Scientific Opinion on the conditions related to "BSE Negligible risk (closed) bovine herds" adopted by the Scientific Steering Committee at its meeting of 22-23 July 1999

The conditions related to "BSE Negligible risk (closed) bovine herds"

1. *Terms of reference*

The SSC was requested to deliver an opinion on the following question:

" *Under what conditions could it be considered that the concept of 'Closed herds' (where there are controlled and documented conditions of breeding and slaughter), offers the same guarantees as the so called 'BSE-free regions'? It is understood that these 'Closed herds' may not necessarily be themselves situated in 'BSE free regions'."*

A working group was established by the TSE/BSE ad-hoc group to put together the scientific basis for an opinion on this issue.

2. *Scope of the question*

In the pharmaceutical, medical sector, one of the preconditions for putting animal derived products on the market is that they are derived from safe sources. These might be countries, accepted to be BSE-free. However, countries may have or have had BSE at some point in time. Therefore, the practical concept of "negligible BSE-risk" herds, sometimes inappropriately called "closed herds" was developed.

In the context of the present report, negligible BSE-risk implies that (1) all the animals alive, at the moment of certification, have never been exposed to any source of infection and (2) have no epidemiological link with TSE cases.

In January 1998, in view of the increased awareness of the potential threat that BSE could be transferred to man not only by food but also via medicinal products and devices derived from cattle, the EC services responsible for preparing regulations on this topic, raised various questions in relation to the use of bovine derived products in the medical sector, including the topic on closed herds which was felt necessary in order to test the basis and validity of the concept.

3. *Definitions*

For the purpose of this report,

- a *herd* is defined as an entity, where cattle are kept under the same conditions.

- a " *Closed-Herd*" is defined as a cattle-herd which is closed with regard to those factors which could introduce the BSE agent into the herd. Following the terminology in the medical sector, and because the term "closed herd" is differently used in the veterinary field, the term "negligible BSE-risk herd" is preferred.

: In normal terminology the term 'closed herd' refers to herds into which no external genetic material is imported. In discussing the mandate, the Working Group agreed, however, that under normal circumstances it is not possible to guarantee that a herd is fully closed without seriously prejudicing the genetic makeup of the herd. A fully closed herd could only be maintained over a relatively short period before further introduction of genetic material proved necessary.

4. *Critical factors in the establishment and maintenance of "Closed herds"*

The following critical factors are identified :

a. Feeding of Meat and Bone Meal (MBM).

It is generally accepted that BSE is mainly, if not entirely, initiated by exposure, to contaminated feed. Inappropriately prepared MBM is assumed to be the most probable source. As long as no guarantee can be provided that MMBM use is made solely of animals or materials [1] that present no risk and that are processed appropriately [2,3] . and without subsequent (cross-) contamination with TSE infectivity, MBM should not be fed. Because of the risk of cross-contamination [4] , continued feeding would also perpetuate the risk of further exposure depending on the degree of infectivity in the MMBM and the amount of infected MMBM fed. However, the SSC recognises that so far herds have been fed with MBM (e.g., from fish or poultry), but recommends that in the future all animal proteins should be excluded.

It is therefore proposed that a negligible BSE-risk herd must be able to prove that no M MBM has been fed to any cattle in that herd for at least 8 years. This period is chosen because of the long incubation period of BSE and in order to provide a safety margin in comparison to the average incubation period of 5 years. On the level of an individual animal it has to be guaranteed that it never has been exposed to MMBM. This must be the case for any animal imported into the herd (see below).

In order to guarantee that no MMBM, either directly or indirectly, *i.e.* by cross-contamination of composite feed, has been fed to the herd, detailed records of the diets must be available for the entire period, which would allow the feed and feed ingredients to be traced back to their origins. Proof must be provided that no MMBM could possibly have been fed.

Because the risk of accidentally feeding potentially infected MMBM increases considerably when other domestic species, which normally receive MMBM in their diets, are held in the same herd (pigs, poultry, sheep) this should not be allowed. With regard to cross contamination, reference is made to the opinion of the SSC on this subject (SSC, 25/9/98).

b. Introduction of genetic material.

A second way of introducing the BSE-agent into a herd could be via the importation of genetic material, i.e. live-animals, semen or embryos.

- Semen and embryos:

An opinion of the SSC Vertical transmission of BSE has been adopted on 18-19 March 1999. It considers it unlikely that semen constitutes a risk-factor for BSE transmission and that the risk of transmission of BSE via embryo transfer is low to negligible.

As a precautionary measure no embryos or semen originating from donor animals which developed BSE should have been used in the herd in the previous 8 years. If semen or embryos are used from a donor animal that develops BSE, as a precautionary measure, all progeny (first generation) should be eliminated.

In addition the conditions for safe semen and embryos have to be met in accordance to the requirements defined in the OIE code on BSE, adopted on 21 May 1999.

- Live animals:

Live animals carry the same BSE-risk as their source. Any animal imported from a non-safe source would therefore pose a threat to the BSE-free status of a herd. Due to the theoretical or actual risk of maternal transmission of BSE the offspring of female animals that have, or subsequently develop BSE also constitute a risk. This includes the genetic offspring of the BSE 'at risk' females and unrelated offspring that have been gestated by the BSE 'at risk' female. Thus live animals of any age should not be imported into the herd unless derived from a herd of equal or superior BSE health status. The safest way of importing genetic material is by the use of semen and embryos according to the recommendations in the OIE *International Animal Health Code* chapter on BSE (OIE, 1999) [5].

In view of the risk presented even by a single animal (see above the discussion on hazards) it is proposed that since 8 years onwards, no animal should have been introduced into the 'closed herd' unless sourced from a herd with an equivalent status or from a country or region classified as "negligible till zero BSE-risk". For herds established for less than 8 years, all animals must come from such safe sources of an equivalent standard as mentioned above.

c. Vaccines and veterinary medicaments

Although there is presently no direct scientific evidence cattle-to-cattle transmission of BSE the risk can not be excluded, because of the analogy to human CJD and vCJD (e.g. the growth hormone cases) and because there are recent reports of scrapie being transmitted to sheep and goats in Italy with a *Mycoplasma agalactiae* vaccine being implicated as the means by which the animals became infected. (Capucchio *et al,* 1998; Agrimi *et al,* 1999) [6] . The vaccine was prepared from homogenised sheep materials including central nervous system tissues. In the United Kingdom there has been a similar incident in the early 1930s with sheep vaccinated against louping ill in which the vaccine was prepared from sheep brain (Gordon, 1946; Greig, 1950) [7] . Special risks can be attributed depending of the origin of the material (bovine or not, geographical region, SRM used or not, etc.). However, vaccines produced in accordance with requirements of the CVMP, are regarded to be safe with respect to the risk of transferring BSE.

d. Other feed components than MMBM

According to the opinions of the SSC on the safety of tallow, gelatine and hydrolysed proteins, these products could constitute a certain risk if they are produced from BSE-contaminated bovine sources. Even if this risk is regarded to be low as long as the conditions for the safe production stipulated by the SSC are respected, a certain risk remains due to the unavoidable uncertainty about the source of the original raw material. It is therefore important that the animals in a negligible BSE-risk herd are not fed these products. For the same reason, feed of unknown origin, such as waste food, should not be given in 'negligible BSE-risk herds'.

5. *Information needed for establishing and maintaining the status of a "negligible BSE-risk herd"*

a. Disease history.

Due to the long incubation period of BSE and the late appearance of clinical signs, the occurrence of BSE in the past could point to a certain risk that more than the affected animal (particularly one born in the same birth cohort) had been exposed to the BSE-agent and are still alive in the herd. Only if the case was 8 years or more ago, and exposure of the animals in the herd to the BSE-agent through feed or maternal transmission since then can be excluded, is the risk of hidden BSE, (i.e. pre-clinical cases) remaining in the herd, considered to be negligible.

It is therefore concluded that in the previous eight years, or since its establishment of the herd (whatever is shorter), no BSE case must have been diagnosed in the herd. Also all animals showing signs of neurological disorders should be examined to exclude the possibility of infection with BSE. Where possible an alternative diagnosis should be available. Whenever such disease did not respond to treatment, or the animal died, a *post-mortem* examination and testing for BSE by an approved method at an approved reference laboratory is essential. However, it will not always be possible to arrive at a definite diagnosis for all cases of neurological disease.

With respect to certification of previous cases of BSE there may need to be some degree of interpretation. Depending on whether the case was homebred or purchased, and for the latter depending on how soon after purchase the animal was clinically affected, the statement on past BSE history does indicate the extent to which the herd has been at risk of exposure, and under veterinary supervision. In other words, it supports statements relating to the absence of risk *via* feed or animal movements.

On clinical and *post-mortem* examinations, it is essential to detect affected animals as soon as possible in view of their potential to donate tissues or fluids which could be administered to humans parentally. In the absence of significant experience of BSE it is perfectly possible however that farmers and even veterinarians will fail to recognise some of the signs of BSE and in such circumstances a *post-mortem* examination of animals that do not recover could provide additional reassurance that the disease is not BSE.

For newly established herds, sufficient guarantees have to be given that the herd is constituted only from animals from a country of negligible to zero BSE-risk or from herds of an equivalent status.

If a BSE case is detected in a 'negligible risk herd', the herd can no longer been considered as ' negligible risk herd'.

As a precautionary measure it is recommended that in a "negligible BSE-risk herd" brains from all bovines from the herd, that have died or have been slaughtered at an age over 1 year [8] , must be examined in an approved reference laboratory, using at least one immunological test for the detection of PrP^{sc} (Western blotting, immunocytochemistry). [: If animals are sold on to another owner, not a negligible risk herd, it will be difficult to guarantee that the brain is examined at slaughter or death. Therefore in practice animals leaving the herd might have to be killed at that time unless they go to another negligible risk herd.] Once available, pre-clinical *in vivo* tests should be applied on a regular basis dependent on the capacity of the test to detect infectivity in the early stages of incubation.

This recommendation is based on the results of the testing of cohorts of BSE affected animals, carried out by the Irish and Swiss authorities. In both instances some animals have been detected in the pre-clinical stage of infection.

b. Records, surveillance, and management

Without good records it would be impossible to certify the past health status of a herd and to verify that the cattle originating from the herd have not died elsewhere.

Therefore, for the last 8 years or since herd establishment (whatever is shorter) complete records of births, deaths and all movements of the individual animals are needed. They must allow the fate of all animals that have resided in the herd within the past eight years to be determined. To this end it is essential that for at least eight years, each animal must have been identified and monitored beyond doubt. For animals which have entered the herd during the past 8 years, records must allow their tracing back to the natal herd, in order to allow an assessment of their status with regard to BSE, especially with respect to their birth cohort.

Veterinary surveillance of the herd should be of such level that guarantee is given that all cases of neurological disorders for which BSE cannot be excluded, are immediately recognised.

The management of the 'negligible BSE-risk herd' must be such that this herd is separated totally from other herds, and must ensure that physical contact with cattle from other herds is avoided as well as contact with potentially infected materials and other domestic species, especially sheep. The latter is to avoid a hypothetical exposure to BSE infectious material (i.e. placenta from TSE (BSE)-infected sheep).

Unless reared in complete isolation and kept under separate (e.g., feeding, grazing, ...) conditions or unless a total ban on the use of MMBM is in place, chickens and pigs should not be on the same premises as the 'closed herd' because of the possibility of accidental feeding of cattle with pig and poultry feed containing MMBM.

6. *Further conclusions*

If a herd complies, in addition to the recommendations formulated in the previous sections, with the following conditions it may be classified as a negligible BSE-risk herd, providing the same degree of safety as sourcing from a BSE-free (negligible BSE-risk) country or region:

- The feed provided to the herd during the last 8 years (or since establishment, whatever is shorter) must be fully documented, allowing the tracing of any feed back to the producer and hence allowing verification of its composition.

- For each animal that resided in the herd during the last 8 years complete identification and movement records must be available, to allow the tracing of those that entered the herd to all herds, including the natal herd and any herd, in which they have previously resided [9] . As far as possible animals should also be traceable after having left the herd, at least to their herds of residence during the 6 months following their departure, unless slaughtered sooner. In the latter case they

should be tested for BSE infectivity.

- If a herd is established for less than 8 years, each animal comprising it must either be sourced from a "BSE negligible risk" country or herd free of the disease for at least 8 years and complying with all the other rules.

- A complete record of clinical disease investigated and treatments received should be kept for each animal. In the case of neurological diseases which did not respond to treatment, a complete examination for the presence of BSE must be documented. Any inconclusive treatment or diagnosis has to be assumed as a BSE-suspect and hence the two strategies described above under "Disease history" have to be considered.

It is recommended to submit all animals older then 12 months at slaughte *r* to the best test available for the detection of BSE infectivity.

The recommendations made by the SSC in its various opinions on safety of ruminant-derived products, geographical risk, intra-species recycling, vertical transmission, fallen stock, etc., remain valid and are also applicable to "closed herds".

7. *Acknowledgements*

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[1] See also the SSC's opinion on the Intraspecies recycling of pigs, poultry, fish and ruminants.

[2] See the SSC opinion of 26-27 March 1998 on The safety of meat and bone meal from mammalian animals, naturally or experimentally susceptible to Transmissible Spongiform Encephalopathies. See also the SSC's updated scientific report of 24-25 September 1998 on The safety of meat-and-bone meal derived from mammalian animalsfed to non-ruminant food-producing farm animals

[3] Poultry fed with TSE contaminated feed may carry infectivity in their digestive tract. Therefore, if MBM is produced from poultry, feeding with such MBM should stop for a number of days before slaughter so that the materials can be digested or excreted.

[4] See the SSC opinion of 24-25 September 1998 on Mammalian derived meat and bone meal forming a cross-contaminant of animal feedstuffs.

[5] OIE (1999). International Animal Health Code chapter 3.2.13 on BSE. Adopted on 21.05.99, Paris.

[6] Agrimi U., Ru G., Cardone, F., Pocchiari, M, Caramelli, M., 1999. Epidemic of transmissible spongiform encephalopathy in sheep and goats in Italy. The Lancet 353, 560-561.

Capucchio MT, Guarda F, Isaia MC, Caracappa S, Di Marco, V., 1998. Natural occurrence of scrapie in goats in Italy. The Veterinary Record, 143, 452-453.

[7] Gordon, W.S., 1946. Advances in veterinary research: louping ill, tick-borne fever and scrapie. Vet Rec 58, 516-525.

Greig, J.R. ,1950. Scrapie in sheep. J Comp Path, 60, 263-266.

[8] See SSC opinion adopted on 24-25 June 1999 on "The risks of non conventional transmissible agents, conventional infectious agents or other hazards such as toxic substances entering the human food or animal feed chains via raw

material from fallen stock and dead animals (including also: ruminants, pigs, poultry, fish, wild/exotic/zoo animals, fur animals, cats, laboratory animals and fish) or via condemned materials."

[9] For practical purposes it might be advisable to allow only animals that moved directly from their natal herd into the closed herd without intermediate steps and provided the natal herd also complies with the closed herd criteria.