TAFS

INTERNATIONAL FORUM FOR TRANSMISSIBLE ANIMAL DISEASES AND FOOD SAFETY
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TAFS[1] Position Paper on Testing of Cattle for BSE – Purpose and Effectiveness

Large scale testing of cattle for BSE has now been established in many countries, starting in Switzerland in 1999, and followed by the European Union in 2001. Similar programmes have subsequently been introduced in other countries. This position paper explains some of the background to such testing, especially in relation to its purpose and effectiveness, and possible future developments. **It also emphasises the fact that the key measure to protect consumers is the removal of Specified Risk Materials, rather than testing. Further details of SRM controls and their background can be found in a separate TAFS position paper.**

For the purposes of this document, testing means the collection of a sample of brain tissue after death or slaughter, and its examination with a commercial "rapid test".

Why are countries required to test cattle for BSE?

- The main purpose of testing is to identify whether BSE exists in a country, and if so, the likely numbers of infected cattle. This is to supplement compulsory reporting of clinically affected suspects, and is particularly important where farmers and veterinarians may have difficulty in recognising BSE. Diagnosis of BSE in the live animal requires experience, and early signs of abnormalities may either be missed, or their significance not recognised. Farmers may therefore slaughter or sell such animals without ever suspecting that they are affected with BSE. Testing has been effective in identifying the first case of BSE in several countries thought to be free of the disease. World-wide statistics arising from surveillance are available through the OIE or World Animal Health Organisation(16).
- By determining how much BSE exists, especially when monitored over a sufficiently long period of time, the testing can give an indication of the effectiveness of measures introduced to control BSE. In other words, a declining prevalence indicates that controls are working. If cases continue to occur for long periods after controls have been introduced, it may mean that controls are not totally effective.

[1] TAFS is an international platform created by a group of scientists, food industry experts, animal health regulators, epidemiologists, diagnosticians, food producers, and consumers. Its purpose is to establish and maintain lines of communication for the dissemination of reliable information to the public that can maintain confidence in the safety of food with regard to Transmissible Animal Diseases (TAD).

- The scale of testing has also enabled the detection of apparently new forms of BSE, in small numbers, colloquially referred to as "atypical BSE". A separate TAFS position paper is available on "atypical BSE"
- In some countries testing of cattle at slaughter is also introduced to increase consumer confidence in the consumption of beef and other products produced from cattle. The removal of positive cattle from the human food chain is claimed to provide a degree of protection to consumers. Clinically suspect cattle are already excluded from the food chain.

Are all cattle tested?

- No. In Europe, the primary target for testing of cattle slaughtered for human consumption is cattle aged over 30 months at the time of slaughter. This age was chosen from experience in the British epidemic that the brain and spinal cord of infected cattle over 30 months are more likely to be infectious, and test positive, than in younger animals.
- Some countries (eg Germany, France, Italy, Spain) have at times included animals aged over 24 months in the testing programme, while Japan, tested all ages in the early days of its surveillance programme. From 2005 the Japanese government no longer required the testing of cattle under 21 months of age, but allowed local authorities to continue should they prefer to do so. That continues to be the position at the beginning of 2009.
- Two other categories of cattle are also targeted for testing. The first, called fallen stock, which are cattle that are sick and die or are culled on farm, do not enter the human food chain. They are normally destroyed by incineration or rendering, or occasionally buried on farm. Such animals over 30 months of age have been shown to have a higher probability of testing BSE positive than animals slaughtered for human consumption. Animals over 24 months in this group weretargeted for testing, but as discussed below, this can change.
- Secondly, a category of cattle called "casualties" are also considered to be a good target population for the detection of BSE. These animals may be suffering from some abnormality, but have been certified by a veterinary surgeon as being fit for human consumption. Cattle with broken legs are an example of such animals. Broken legs or other injuries can arise as a result of excessive kicking on the part of the cow due to infection with BSE. In the EU, casualties (defined as cattle subject to emergency slaughter or found sick at ante-mortem inspection) over 24 months of age were tested for BSE. Some countries ban the consumption of casualties, in which case they will then be destroyed and tested along with fallen stock.
- Testing of fallen stock and casualties is the most cost-effective approach of finding BSE infected animals in that fewer animals have to be tested for each positive detected. Together they are commonly referred to as "risk animals."
- None of the categories and age-groups referred to above are absolute. It is essential that they are reviewed from time to time to consider whether they remain appropriate. (See below)

Is it necessary to test all ages of cattle?

- No. Some countries have at times introduced such a policy (eg Japan), but it is extremely expensive while doing little to increase the likelihood of finding positive cattle.

- Experience in the United Kingdom suggests that most infected cattle die of BSE at between four and six years of age, with an average of 60 months[19] although some may be much older. Research on sheep naturally infected with a similar disease called scrapie, or mice experimentally infected with scrapie, suggested that the brain would be infected by approximately mid-way in the incubation[4, 7, 10, 14]. Translated into cattle this would be approximately 30 months of age if it is assumed that calves become infected in the first few months of life. Small numbers would of course be positive before this age. Surveillance in Germany has shown this to be possible, and the age at testing in that country was reduced to 24 months as a result. Japan has had a similar experience. Indeed the youngest BSE case ever detected was clinically affected at 20 months of age in the United Kingdom, and may represent the extreme end of the age range of affected cattle.
- Brains of cattle experimentally infected with 100g of BSE-infected brain in two separate challenge studies in the United Kingdom have tested positive only at 32 and 30/33 months after infection[1,8,18,], although one of these studies also demonstrates that the brain is infectious shortly before it tests positive by rapid tests[8]. A German study has confirmed however that there is considerable variation between animals challenged at the same age, and occasional animals may be positive before 30 months[11]. In that study, the lower limit detected after an oral dose of 100g was 24 months post- infection. Perhaps more realistically, following a dose of 1g only, and more likely to represent natural exposure levels, brain was found to be positive at 44 months post-infection[1].
- Further research data from the United Kingdom on BSE-infected cattle suggests that the brain is actually not infectious until a much later stage of incubation than seen in sheep and mice with scrapie. It seems as if this may only be in the six to 12 months before the onset of clinical disease. This suggests that for the majority of infected cattle the selection of 30 months as the age above which cattle are tested is appropriate, and cautious. In other words, it should detect the vast majority of infected cattle that are approaching the onset of clinical disease [1, 3, 9, 18].
- Selection of just a proportion of cattle to test, such as fallen stock, casualties and healthy animals over 30 (or 24) months of age when killed, makes best use of limited resources in establishing a large testing programme, particularly in countries with low BSE risk. In other words, in order of probability of detecting positive cattle, testing could be focused on cattle exhibiting clinical signs compatible with BSE, fallen stock/casualties, or apparently healthy cattle over the age of 30 months when slaughtered. The ideal mix of cattle to be sampled will vary from country to country, but the testing of healthy cattle is not an appropriate substitute for the testing of the other categories.

What tissue is tested?

- Brain (particularly the part referred to as brain stem), or sometimes spinal cord, are the preferred tissues to test. This is because these tissues, along with the eye, are the only tissues found to be consistently positive in naturally infected cattle. The tests used have also been optimised to work on brain.
- In experimentally infected cattle, in addition to central nervous tissue, the lower small intestine is also infected, but it is inconsistently positive and it is not yet possible to perform tests with any confidence on this tissue. It has not proved possible to demonstrate this infectivity in the intestine of naturally infected cattle. Traces of infectivity have been detected in tonsil and bone marrow of experimentally infected

cattle, but these results do not indicate that either tissue is an appropriate alternative for testing.

- More recently, tests carried out on peripheral nerves of cattle clinically affected with BSE[2,12,13,15] have confirmed that at late stages of incubation some nerves are positive, but much less so than brain. So again they do not represent optimal targets for testing.

Is this effective in detecting all infected cattle?

- No. Only a proportion of infected cattle will be detected by the testing of brain. As explained above in selecting the age of cattle to test, infectivity appears to reach the brain and spinal cord only relatively late in the incubation period. Consequently, an animal in the early stages of incubation will test negative despite being infected.
- This problem could be overcome if the intestine could be tested as described above, but that is not yet possible with current tests.

If all infected cattle cannot be detected by this means, why bother to test at all?

- Because the primary purpose of testing is to improve our understanding of how much BSE exists in the cattle population, the inefficiency of the testing approach is outweighed by the additional information gathered, over and above reliance on the detection of clinically affected cattle. Taken together they give a better indication of the scale of the problem, and whether or not measures introduced to control BSE are effective. Ideally surveillance results should indicate that cattle born after the introduction of control measures are either not infected or far less likely to be infected than cattle born before the measures.

If only a proportion of infected cattle can be detected, does testing provide significant consumer protection?

- The extent to which testing increases consumer protection is still open to question, especially if other protective measures are in place (see below).
- It is conceivable that tissues not previously recognised as infected may still be found as research continues. Infectivity levels are expected to be extremely low, and undetectable with the tools used so far. If these tissues were otherwise consumed then the destruction of the carcase would afford the consumer a greater degree of protection. If the tissues are not sufficiently infectious to pose a health risk, and/or are not consumed, then the additional protection provided may be nil.
- Recent results from Japan and Germany confirm this point[2,12,13,15], with positivity or infectivity being detected in some peripheral nerves that would not normally be removed as SRM. The amount of infectivity present is low, and considered be up to 1000-fold lower than the brain. Unpublished evidence suggests that these become positive only after the brain and spinal cord. This therefore confirms that testing and removal of positive animals does provide some additional, as yet unquantifiable, protection to consumers over and above that provided by removal of SRM. Given that detection of positivity or infectivity in some peripheral nerves coincides with the onset of clinical signs, it is probable that such animals would be detected before slaughter, and therefore excluded from the food chain.

What alternatives are there to testing of cattle slaughtered for human consumption?

- In most countries, testing of cattle at slaughter is only one of several lines of defence to protect the consumer.
- The first critical step is the exclusion of all clinically affected cattle from the human food chain. These should be reported to the authorities, killed and destroyed. Inspection of animals as they enter the abattoir for slaughter will identify some affected cattle that may not have been detected on farm. Indeed, transportation to the abattoir often triggers more obvious clinical signs in affected animals. These will be destroyed.
- Finally, in most countries where BSE has been recognised, the key protective measure is the removal from the human food chain of tissues that are expected to contain the greatest amounts of infectivity. Such tissues are currently called Specified Risk Materials. These are described more fully in the TAFS position paper on SRM.
- When SRM are removed they are destroyed, and thereby also excluded from animal feed as well. This measure therefore protects both humans and animals.

What tests are used?

- Since 1999, when the European Commission first evaluated new rapid screening tests, there have been further rounds of evaluation and approval. In addition, the OIE has also started to offer evaluation of tests for more global use.
- All allow the completion of testing of cattle within a matter of hours from death, thus enabling abattoirs to await the results before carcases are released for human consumption. All parts of positive animals are then kept separate and destroyed.
- Although test manufacturers make claims about the relative merits of their tests, all are considered to be appropriate for the purpose. None have been shown to guarantee the detection of animals earlier in the incubation period than the others. Criteria for selection of tests for use in a particular country therefore take into account the skills and resources in that country for conducting testing, the volume of testing to be done, and test cost price.
- Because of the constantly evolving nature of this area, with approvals having taken place in the EU, Japan, USA and Canada, it is not possible to list all approvals in this document. Most of the tests used in N America and Japan are related to those approved in Europe, and are essentially identical. The OIE Reference Laboratory at the Veterinary Laboratories Agency[17], UK therefore maintains lists of approved tests, or links to approval sites in other countries where accessible, that will enable readers to further investigate what is available on the market.
- Any animals found positive by the use of such tests are subjected to further testing at National Reference Laboratories using internationally recognised confirmatory tests. Carcases will already have been removed from the food chain before this as a precautionary measure.

Will testing continue indefinitely?

- This is most unlikely as it is extremely expensive and complex to implement. In its discussion document entitled the "TSE Roadmap"[5], the European Commission estimated that between 2001 and 2004 it cost 1.56 million euros to detect each case by testing in the healthy slaughter population, but this rose to 64 million euros/case for animals aged under 48 months. As this is an average figure, for countries with very low incidence of BSE the cost was even higher.
- As control measures take effect, these costs will rise even in older testing groups, while in parallel the risk to consumers is falling towards zero.

- The TSE Roadmap therefore began a public debate in Europe about planning a future strategy that will maintain protective measures for both consumers and animals, but at a cost that is proportionate to the risk.
- As anticipated by the TSE Roadmap, the review process was taken forward in 2008 when the European Commission consulted the European Food Safety Authority on options for alternative testing strategies. In recognition of the falling prevalence of BSE in EU countries where controls were tightened at the end of 2000, the Commission asked EFSA to consider the implications of raising the target age for testing in both healthy and risk categories of cattle. The EFSA Opinion offered estimates for the consequences of increasing the minimum age at testing by 12 month intervals to an upper limit of 60 months.
- In summary, the EFSA Opinion(6) considered options of raising the age at testing to 36, 48 or 60 months in healthy cattle, and 30, 36, 48 and 60 months for risk animals. As recognized earlier in this paper, falling prevalence of BSE in EU15[2] countries confirmed the effectiveness of measures introduced at the end of 2000 (newer Member States where control measures have not been in place for as long as in EU15 countries were excluded as further time was needed to provide evidence of effectiveness).
- For healthy cattle, the Opinion estimated that fewer than two cases would be missed in all EU15 countries if the age at testing was increased to 36 or 48 months, and fewer than three missed if the age was raised to 60 months.
- For risk animals, less than one positive animal would be missed by raising the age at testing to 30, 36 or 48 months, or fewer than three cases if raised to 60 months.
- As a result, the Commission recommended that EU15 countries could apply to increase the age at testing in both surveillance streams to 48 months in 2009. Following consultation with the European Parliament, and by national authorities, the age at testing in EU15 countries has been raised to 48 months in 2009. Some may decide not to apply this flexibility across all surveillance streams.
- In future, similar changes can be anticipated in the remaining EU countries, and the age limit may be raised further in the EU15 countries, but all changes will continue to be subject to ongoing review of surveillance and enforcement data throughout the EU.

[2] EU15 countries – Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, The Netherlands, Portugal, Spain, Sweden, United Kingdom.

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