STATEMENT ON THE POTENTIAL HUMAN HEALTH RISK FROM CHANGES TO CLASSICAL SCRAPIE CONTROLS

Issue

1. The Department for Environment Food and Rural Affairs (Defra) requested advice on the potential risks to human health of changes to the control measures employed when transmissible spongiform encephalopathy (TSE) infections are found in small ruminant (sheep and goat) flocks/herds.

Background

2. In 2001, Regulation (EC) No.999/2001 established rules for the prevention, control and eradication of certain animal TSEs. In 2003, Regulation (EC) No.1915/2003 amended the former regulation to introduce compulsory controls on sheep flocks and goat herds affected with TSEs. The amended legislation required the culling and destruction of the whole flock/herd on confirmation of BSE in a sheep flock or goat herd. Following identification of classical scrapie in a sheep flock, the whole flock, or those sheep in the flock with genotypes considered more susceptible to classical scrapie, had to be destroyed instead of being slaughtered for human consumption. The latter option allowed sheep of relatively classical scrapie-resistant genotypes, from flocks known to be affected, to be slaughtered for human consumption. For goat herds, whole herd culling was the only option.

3. In 2006, the European Commission proposed (and in 2007 put into legislation) changes to the culling requirements outlined in the TSE Roadmap that set out proposals to relax TSE controls whilst maintaining public health protection[1]. The changes allowed the slaughter for human consumption of small ruminants from flocks/herds where a TSE had been identified provided that (i) the TSE had been determined to be classical or atypical scrapie and not to be bovine spongiform encephalopathy (BSE) by discriminatory testing of the index case and (ii) the animals, if aged

[1] European Commission (2005) TSE Roadmap.
http://ec.europa.eu/food/food/biosafety/bse/roadmap_en.pdf

over 18 months, had first tested negative for TSEs using European Union (EU) approved rapid tests.

4. As a result of scientific opinions on the sensitivity of the biochemical tests to detect and discriminate between BSE and forms of scrapie and on the potential transmissibility of classical scrapie to humans[2,3,4], objections have been raised to the changes on the grounds that they may pose an increased risk to human health disproportionate to the benefits.

5. To address the Defra request, SEAC considered the scientific opinions and other data[5].

TSE tests in small ruminants

6. Rapid tests used for EU surveillance to detect TSEs in small ruminants are based on finding abnormal prion protein (PrP^{Sc}), an established marker for TSE infection, in the brain of infected animals. However, as PrP^{Sc} accumulates in the brain relatively late in the incubation of TSEs, animals in the early stage of infection, when PrP^{Sc} accumulation is restricted to the periphery, are not identified.

7. Discriminatory tests to differentiate between classical scrapie, atypical scrapie and BSE in small ruminants are based on resolving the structural forms of PrP^{Sc} associated with each of these diseases. Evaluations of these tests conducted to date suggest they are robust in discriminating between BSE, classical and atypical scrapie[6,7]. However, their ability to identify one disease when another is present concurrently has not been rigorously ascertained.

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[2] Opinion of the French Food Safety Agency (AFSSA) given on 15th January 2007 on changes to the control measures for sheep and goat herds in which a case of classical or atypical scrapie has been detected. http://www.afssa.fr/Documents/ESST2006sa0343EN.pdf

[3] Opinion of the Scientific Panel on Biological Hazards given on 8th March 2007 on certain aspects related to the risk of transmissible spongiform encephalopathies (TSEs) in ovine and caprine animals http://www.efsa.europa.eu/EFSA/Scientific_Opinion/biohaz_op_ej466_tse_ovine_caprine_en.pdf

[4] KOM AG TSE opinion. No reference available.

[5] SEAC paper 99/3. Scientific basis for classical scrapie controls. http://www.seac.gov.uk/papers/99-3.pdf

[6] Stack *et al.* (2002) Differentiation of prion protein glycoforms from naturally occurring sheep scrapie, sheep-passaged scrapie strains (CH1641 and SSBP1), bovine spongiform encephalopathy (BSE) cases and Romney and Cheviot breed sheep experimentally inoculated with BSE using two monoclonal antibodies. *Acta Neuropathol.* 104, 279-286.

[7] Stack *et al.* (2006) Monitoring for bovine spongiform encephalopathy in sheep in Great Britain, 1998-2004. *J. Gen. Virol*. 87, 2099-2107.

TSEs in small ruminants

8. Classical scrapie is a disease of small ruminants that has existed in the UK for over two hundred years. Since the introduction of small ruminant TSE controls in the United Kingdom (UK), the incidence of classical scrapie has fallen appreciably[8]. Data from UK surveys of culled animals from classical scrapie affected flocks suggest that the level of infection of other animals in the majority of affected flocks is relatively low[9]. This suggests that under most circumstances the disease does not spread rapidly through a flock and the majority of animals in an affected flock are uninfected.

9. It is unclear whether atypical scrapie is a new TSE of small ruminants or whether it had existed for some time before it was first recognised. There is evidence that it has been present in the UK since at least 1989[10]. Epidemiological evidence suggests that atypical scrapie is widely distributed geographically within Europe and that it is of low transmissibility. Thus, it seems most likely that, like classical scrapie, atypical scrapie has existed for some time and is not a new epidemic[11,12]. Classical and atypical scrapie have been found to co-exist in some sheep flocks[11].

10. BSE has never been found in UK sheep despite extensive passive and active surveillance. Discriminatory testing of confirmed cases of TSEs in small ruminants has established them to be classical or atypical scrapie. Discriminatory tests have also been applied to isolates from a small number of historic goat TSE cases. An isolate from one goat from Scotland born in 1987, originally diagnosed as scrapie in 1990, gave results consistent with BSE by a single test (differential immunohistochemistry)[13]. As this is insufficient to definitively classify the infection as BSE, mouse transmission studies with material from this isolate to confirm the diagnosis of BSE are underway but are not yet complete. However, even if confirmed as BSE, this is a historical case born prior to the introduction of the ruminant feed ban and thus could have been exposed to BSE-contaminated feed. TSE infections have not been detected in the progeny or subsequent generations of this goat[13].

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[8] Defra statistics. http://www.defra.gov.uk/animalh/bse/statistics/scrapie/inciden.html
[9] Unpublished Veterinary Laboratories Agency data.
[10] Bruce *et al.* (2007) Nor98-like sheep scrapie in the United Kingdom in 1989. *Vet. Rec.* 160, 665-666.
[11] SEAC Sheep Subgroup (2006) Statement on atypical scrapie. http://www.seac.gov.uk/pdf/positionstatement-sheep-subgroup.pdf
[12] SEAC Sheep Subgroup report of 2007 meeting. http://www.seac.gov.uk/committee/sheepsubgroupreport07.pdf
[13] SEAC 86 minutes (2005) paragraphs 66-79. http://www.seac.gov.uk/minutes/final86.pdf

11. Estimates suggest the prevalence of BSE in UK sheep is very low if it is present at all[12]. Data from surveillance of UK goats are too limited to allow similar estimates of the prevalence of BSE in goats. However, with the exception of the suspected (but not confirmed) case described above, no further suspected or confirmed cases of BSE have been found in UK goats. It is possible that BSE could co-exist with classical or atypical scrapie in small ruminants and not be identified by discriminatory tests. However, as classical scrapie is rare, and BSE on its own has never been found in sheep and possibly once historically in a goat, the probability of mixed infections occurring in the current UK flock/herd is very low or negligible[12].

Links between classical or atypical scrapie and human TSEs

12. Classical scrapie has been present in the UK for more than 200 years without any apparent association with human TSEs. Human TSEs exist in countries such as Australia and New Zealand with no reported cases of classical scrapie, although small ruminant TSE surveillance in these countries is relatively limited. As establishing epidemiological links between comparatively rare diseases is very difficult, a link between human TSEs and classical scrapie may never be able to be completely ruled out. Authors of the two epidemiological studies[14,15] that have examined risk factors for sporadic Creutzfeldt-Jakob Disease (sCJD) have dismissed a link between classical scrapie and sCJD. Although, these data could be interpreted differently to suggest a potential link, this could be a chance association arising from biases inherent in the design of these retrospective studies.

13. Epidemiological data suggest that atypical scrapie may have existed for some time. If this is the case, it, like classical scrapie, has probably existed with no apparent association with human TSEs. However, the possible emergence of atypical scrapie as a new disease with potential public health implications cannot be entirely ruled out and further information is required about the possible transmissibility of this disease to humans.

[14] van Duijn *et al.* (1998) Case-control study of risk factors of Creutzfeldt-Jakob disease in Europe during 1993-95. *Lancet.* 351, 1081-1085.
[15] Brown *et al.* (1987) The epidemiology of Creutzfeldt-Jakob disease. Conclusion of a 15-year investigation in France and review of the world literature. *Neurology*. 37, 895.

Risk assessment

14. No cases of BSE in sheep, and only one suspected (but not confirmed) case of BSE in goats, have been found in the UK. Estimates suggest that the prevalence of BSE in UK sheep currently is very low if it is present at all[12]. There are too few data to support similar estimates of the prevalence of BSE in goats in the UK. If BSE is present in UK sheep or goats, measures are in place to limit its spread (i.e. feed controls and controls on the TSE affected flocks or herds in which a TSE case has been confirmed). It is possible that classical or atypical scrapie may prevent the detection of BSE in co-infected animals. However, the prevalence in small ruminants of such co-infections is likely to be even lower than that of BSE on its own (see paragraph 11)[12]. Thus, although the presence of BSE in a TSE-affected flock/herd cannot be ruled out by discriminatory testing of the index case, the risk that undiagnosed BSE infections may be released inadvertently into the food chain as a result of the changes to the classical scrapie controls is likely to be very low or negligible.

15. As the rapid testing method used for EU surveillance cannot detect TSE infections at the stage of incubation prior to accumulation of PrP^{Sc} in the brain, the changes to classical scrapie controls are likely to increase the number of subclinically infected animals that enter the human food chain. It is not possible to quantify the increase as it depends on how widespread infection may be in affected flocks/herds and the unknown level of subclinical infection in the very large proportion of small ruminants slaughtered for human consumption that are not currently tested for the presence of TSEs. Given the apparent slow rate of transmission within a flock, any increase in the number of classical scrapie infected animals entering the food chain from an affected flock is likely to be low and should be considered in the context of the background level of human exposure to classical scrapie arising from animals not currently tested.

16. There is no firm evidence for a link between human TSEs and classical scrapie. Although a link cannot be ruled out, even if there is a link, the human health risk from classical scrapie must be very low and result in very few human TSE cases per annum. This is because the incidence of human TSEs is very low and relatively constant world-wide (around one case per million people per year) showing that there must be at least a substantial, if not complete, barrier to transmission of classical scrapie to humans. Although it is not possible to quantify any increase in risk that would arise from the changes to classical scrapie controls, the increased risk is

highly unlikely to be greater than the risk before classical scrapie controls were introduced. Indeed, given the apparent effect of the National Scrapie Plan (NSP) on reducing the incidence of classical scrapie in the UK, the risk, if it exists, is likely to be appreciably lower than prior to the implementation of the NSP controls.

17. It is possible that the changes to the EU controls may increase the level of atypical scrapie entering the food chain from classical scrapie affected flocks with concurrent atypical scrapie infections. However, given the low occurrence of atypical scrapie within flocks, any increase in the potential human health risk from atypical scrapie is likely to be very low.

Summary

18. Although the changes to the classical scrapie controls may increase the potential risks to human health from small ruminant TSEs, any risk that is present is currently very low or negligible and any increased risk likely to be very low or negligible. For classical scrapie, any increase in potential risk will be less than the long-term historic risk prior to the introduction of small ruminant TSE controls. A risk-benefit analysis is required to determine the proportionality of the changes in controls with respect to the increased potential risks. Such an analysis is not within the remit of SEAC.

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