Afssa – Mandate No. 2006-SA-0343

Afssa – Mandate No. 2006-SA-0195

Maisons-Alfort, 15 January 2007

OPINION

of the French Food Safety Agency (Afssa) on changes to the control measures for sheep and goat herds in which a case of classical or atypical scrapie has been detected

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In a letter received on 26 June 2006, the Agence française de sécurité sanitaire (Afssa) [French Food Safety Agency] received a request dated 22 June 2006 from the Direction générale de l'alimentation (DGAl) [Directorate General for Food] for an opinion on the possible changes to the control measures for sheep and goat herds in which a case of atypical scrapie has been detected.
Subsequently, in a letter received on 12 December 2006, the Afssa received a request dated 6 December 2006 from the DGAl for an opinion on the possible changes to the control measures for sheep and goat herds in which a case of classical scrapie has been detected.
These two mandates are based on the proposals made by the European Commission in its TSE Roadmap.

In view of the complementarity of these questions and the response times required due to the meetings of the Standing Committee on the Food Chain and Animal Health (SCFCAH) in January 2007, the two mandates are being covered jointly in this opinion.

1. General context

In a letter dated 22 June 2006, the DGAl requested Afssa for an opinion on the possible changes to the control measures for sheep and goat herds in which a case of atypical scrapie has been detected, based on the proposals made by the European Commission in the TSE Roadmap.
According to the most recent documents submitted to the CES ESST [Expert Committee on TSEs] on 25 September 2006, these proposals imply that when a herd is infected with atypical scrapie – meaning when the index case is characterised as atypical – the herd will not be subject to any eradication measures but will be subject for two years to systematic testing of all animals aged over 18 months which are slaughtered or culled, with no specific restriction on the sale of breeding stock or the consumption of products (carcasses and milk products) from this herd. The system will be supplemented by the identification of all the animals in the herd concerned and by restrictions on movements to the other Member States or third countries.

In a second letter dated 6 December 2006, the DGAl requested Afssa for an opinion on the proposals made by the European Commission in its TSE Roadmap regarding changes to the control measures for sheep and goat herds in which a case of classical scrapie has been detected.
According to the documents submitted to the CES ESST on 21 December 2006, the Member States may choose to apply one of the following options:

A- eradication through total (goats, sheep where applicable) or partial (sheep of susceptible genotypes) slaughter.
The Member States may then decide:

(i) either to destroy the slaughtered animals (measure corresponding to the current control measure),

(ii) or to release these animals for consumption subject to a negative test (test carried out on slaughtered animals over 18 months old).

This new system would be accompanied, in infected herds, and for a period of two years, by:
- the systematic conduct of a rapid test on animals over 18 months (slaughtered for consumption or culled);

- for sheep flocks, the exclusive use of ARR/ARR rams and the introduction of ewes carrying at least one ARR allele (and not carriers of the VRQ allele);
- for goat herds, restocking from "scrapie-free" herds or herds from which scrapie has been eradicated;
- the application of disinfection measures prior to restocking the herd in the case of slaughter.

B – an alternative strategy, for 2 years, based on:

- marking the animals from infected herds;
- the exclusive introduction of ARR/ARR rams or of ewes carrying at least one ARR allele (and not carriers of the VRQ allele) or goats from "scrapie-free" herds or herds from which scrapie has been eradicated;
- restrictions on movement, which would be permitted only to abattoirs (exemption/specialist fattening) except for sheep with the ARR/ARR genotype;
- restrictions on shared grazing;
- the conduct of rapid tests on all animals over 18 months old slaughtered for consumption or culled.

A number of options have also been raised by the European Commission and may be introduced in later versions of the document.
These options principally concern:
- the application of discriminatory tests (BSE/scrapie/atypical scrapie[1]) which could be carried out on index cases only;
- the duration of the measures accompanying the APDI [Arrêté prefectorale de declaration d'infection – Prefectoral Infection Declaration Order] (3 years instead of 2);
- the tests conducted on animals aged over 18 months, which would no longer be exhaustive but conducted on a sampling basis;
- the SRM list which could be extended to the whole head and all intestines;
- the possible restriction on the sale of products from these animals to national markets.

Afssa asked the CES ESST to examine specifically the questions below:

"1) Does the CES consider that products from sheep and goats from herds infected with classical scrapie, slaughtered in the conditions described above, represent an additional risk to public health compared with products from genetically resistant sheep only?
2) In the knowledge that the current surveillance tools for small ruminants at best enable the detection of only a fraction of the flocks infected with a TSE and that the sheep population is composed in part of genetically susceptible animals, can the CES compare the above-mentioned risks with the risk from an "ordinary" animal slaughtered under the conditions currently in force?
3) What measures, in particular as regards the removal of specified risk material or BSE tests, could be recommended to reduce any additional risk which might be identified above?
4) Based on the answers to the preceding questions, could you carry out a comparative analysis of the potential level of risk represented by the eradication strategy compared with the alternative strategy, as regards the animal health and public health issues.
5) Finally, with a view to allowing the consumption of animals from flocks with a TSE outbreak, would it be pertinent to lower the age at which animals are tested, currently suggested as 18 months by the Commission?"

Following the meeting of the CES ESST of 21/12/2006 and electronic validation on 11/01/2007, the committee is issuing the following opinion:

2- Preamble and reminder of previous Opinions

As a preamble, the Committee would first like to recall:

[1] Differentiation between classical and atypical scrapie cannot necessarily be obtained by using discriminatory tests designed to distinguish BSE from other scrapie strains. In France, for example, this differentiation is achieved by using a confirmation western blot which produces a characteristic profile in cases of atypical scrapie.

1) the limitations of the discriminatory tests (BSE/scrapie). In a previous opinion[2] it stated:
"The Committee has stated its position several times on the current limitations of the rapid tests designed to identify the BSE strain in small ruminants. It considers that the actual sensitivity of these tests is not known precisely enough and that a negative result obtained with one of these tests does not enable the presence of BSE in the tested animal to be completely ruled out. Especially since certain studies have indicated that in the case of co-infection with BSE and a strain of scrapie, identification of the BSE may be compromised. Furthermore, rapid tests as they are currently conducted are not capable of identifying animals infected with a strain of TSE during a large part of the incubation period, as they are carried out exclusively on tissue samples from the central nervous system, even though certain tissues (notably lymphoid organs) may contain large quantities of the infectious agent much earlier."

Moreover, the conduct of a discriminatory test solely on the index case in infected flocks in no way guarantees the absence of BSE in this flock (possibility of the co-existence of different prion strains in the same flock), and it is for this reason that, in a previous opinion[3], Afssa has already recommended that all animals slaughtered as part of a control measure should be subject to a rapid test and that secondary cases should be subject to a discriminatory test (BSE/scrapie).

2) that the transmissibility to humans of "classical" and atypical scrapie strains cannot be excluded:
" …the Committee considers that it is quite premature to conclude that strains of TSEs, other than BSE, pose no risk to human health. While there is no epidemiological data to indicate a clear link between sheep and goat scrapie and the human forms of TSE, the variety of strains of TSE which can circulate in small ruminants and the lack of a really convincing prospective study must lead to the adoption of a prudent position on this subject. The discovery, very recently, of atypical strains whose aetiology could be either genetic or sporadic clearly illustrates the uncertainties persisting in this field.
As regards the atypical forms of scrapie, while a large amount of experimental data clearly indicate that they are different from BSE, the data currently available do not permit the hypothesis of transmission to humans to be ruled out."

Consequently, the Committee considers that the release for human consumption of tissue from small ruminants cannot be envisaged in conditions in which it probably or certainly contains significant quantities of infectious agent, even if a discriminatory test indicates that what is probably involved is classical or atypical scrapie.

3- Control measures applicable to flocks in which a case of classical scrapie has been detected.

As already explained in the framework opinion issued by the Committee[4], it has been clearly established that:
(i) in the first months following infection with classical scrapie or BSE, the infectious agent is widely distributed in the peripheral tissue of individuals with a susceptible genotype (non-carriers of an ARR allele);
(ii) in individuals with a susceptible genotype (non-carriers of an ARR allele), removal of the SRM, even when extended to the head and the intestines, does not permit the elimination of all tissue carrying significant levels of infectivity;
(iii) a negative result in a screening test carried out on the obex in no way guarantees the infectious status of a small ruminant in terms of BSE or scrapie.

[2] Afssa opinion of 15 May 2006 on the changes to community regulations proposed by the TSE Roadmap
[3] Afssa opinion of 20 July 2006 on assessment of the risk from the potential presence of BSE in sheep on 20 July 2006
[4] Afssa Framework opinion of 25 March 2005 on the analysis of the risks from transmissible spongiform encephalopathies in the small ruminant sectors, the strengths and weaknesses of the current system and the options for change. Update of the February 2002 Opinion

The Committee also wishes to state that studies carried out in sheep and goat herds infected with scrapie have shown an incidence as high as 10 to 45% of the cohorts (Corbière et al. 2007 forthcoming). These figures show the order of magnitude of the additional risk of infection in a small ruminant born in a scrapie-infected flock.

The three options proposed by the Commission, left to the free choice of the Member States, were examined based on these elements of information.

The first option proposed by the document corresponds to the control measures already in place in France.
- For goat farms, the control measures require the slaughter of the whole herd and its destruction. However, the farmer may choose to join an experimental protocol which involves the conduct of tests *ante mortem* on samples of tonsils[5] from animals aged over 12 months.
- For sheep farms, the control measures require:
(i) genotyping of the entire flock;
(ii) the slaughter and rapid destruction of animals carrying susceptible genotypes;
(iii) the introduction into the flock solely of females carrying at least one ARR allele (excluding the ARR/VRQ genotype) and the use for breeding solely of rams of the ARR/ARR genotype.
These measures are accompanied for three years by:
(i) the conduct of rapid tests on casualty or euthanased animals over 18 months old and on a sample of sheep over 18 months old slaughtered for consumption;
(ii) a ban on the export of live animals (except ARR/ARR).

- The Committee considers that the current control measures, by ensuring the rapid destruction of the individuals from an infected herd with the highest probability of being infected (susceptible genotypes), following herd exposure to the classical scrapie agent, remains the strategy providing the best level of safety for the consumer and offering the best possible control of the animal health issue.

In a second option, the Commission document proposes:
(i) genotyping the entire flock in the case of sheep;
(ii) slaughtering the whole herd (for goat farms) or only animals of a susceptible genotype (for sheep farms);
(iii) releasing the slaughtered animals for human consumption (after removal of the SRM) subject to a negative rapid test carried out on animals over 18 months.

- The Committee finds this option unacceptable. It has been clearly established that a negative result from a screening test conducted on a sample of brain tissue from an animal aged 18 months or over does not guarantee the absence of infectious material in the food produced from that animal. This is especially true when this animal is carrying a susceptible genotype, as illustrated in the examples presented above.

The third option proposed by the document does not involve the genotyping of all individuals, in the case of sheep farms, but proposes:
(i) marking of all animals;
(ii) the conduct, for two years, of rapid tests on all animals over 18 months slaughtered for consumption or culled;
(iii) restriction measures on animal movements.

- In view of the elements already discussed, the Committee considers that these measures:
(i) do not enable the effective limitation of consumer exposure to potentially significant levels of infectivity;
(ii) are likely to promote the persistence of the infection in infected flocks by not eliminating the animals with a susceptible genotype (long-term cohabitation of healthy animals and potentially infected animals).

[5] Afssa opinion of 9 February 2005 on the modalities for putting in place an experimental protocol in the context of a change to the control measures for goat scrapie

4- Control measures applicable to herds in which a case of atypical scrapie has been detected.

The Committee based its opinion on the work of the "Epidemiology of animal TSEs" working group, whose report is appended.

This report, and discussions during the meetings, have raised two important questions regarding:

(i) the possible presence of the infectious agent in the peripheral tissue (even though this presence has not been demonstrated experimentally);

(ii) the possible transmission to other animals, in natural conditions, of this form of scrapie (even though the available data indicate that this transmission would be less effective than that observed for classical scrapie).

These uncertainties complement the concerns as to whether these agents can cross the species barrier, and the human species barrier in particular.
The Committee acknowledges, moreover, that the control measures applied in the case of classical scrapie are not appropriate for atypical scrapie (little or no resistance in animals carrying the ARR allele– low apparent prevalence in infected herds).

During the discussions at the meeting on 21 December and in the e-mail exchanges in early January 2007, differences of opinion emerged within the Committee regarding the possible public health risk posed by atypical scrapie.

Therefore, while all members of the Committee consider the following actions are necessary:
(i) putting in place specific precautionary measures taking account of the above-mentioned uncertainties, these measures may be adapted (reduced, lifted or strengthened) to reflect developments in our understanding of these agents;
(ii) collecting, from the infected herds, the information required for an accurate assessment of the risks from this type of agent,
some members of the Committee consider that, to increase the level of consumer protection, use should also be made of the knowledge acquired on the increased susceptibility of certain genotypes to atypical scrapie, although other members think this measure is excessive.

Consequently, the Committee is recommending that, for herds infected with atypical scrapie, the current control measures should be amended as follows:
(i) the herds should be placed under surveillance for a 5-year period (period covering the almost complete replacement of flock individuals);
(ii) all individuals from infected herds should be genotyped for the four codons of interest (136, 141, 154 and 171);
(iii) in the absence of data on the possibility of transmission in natural conditions, sale of breeding stock to farms with a different status should be prohibited during the surveillance period;
(iv) all individuals from infected herds slaughtered or culled and aged more than 18 months should be tested using one of the rapid tests most suitable for the detection of atypical cases (currently the Biorad and Iddex tests);
(v) all secondary cases detected should be subject to a discriminatory test[6];
(vi) in the event of detection of classical scrapie in one of these secondary cases, the corresponding control measures should be applied;
viii) no restriction on contacts with other flocks should be imposed.

In addition to these measures, the majority of the Committee (10 people) is recommending that, in view of the increased susceptibility to atypical scrapie associated with the AHQ and AFRQ alleles, animals carrying these alleles should not be released for human consumption but destroyed at the end of their economically useful life. In the event of the detection of classical scrapie in one of these secondary cases, animals with the genotype ARR/AHQ and ARR/AFRQ should be kept from human consumption during the 5 years of the surveillance period.

[6] Differentiation between classical and atypical scrapie does not necessarily result from the use of discriminatory tests designed to distinguish BSE from the other scrapie strains. In France, for example, this differentiation is achieved using a confirmation western blot which produces a characteristic profile in cases of atypical scrapie.

A minority of the Committee (7 people) considers this latter measure too harsh. They feel that if the whole flock is to be genotyped for the four codons of interest, in the interests of acquiring knowledge and to be able subsequently to adapt the measures to reflect the risk, there is no justification for keeping animals carrying at least one AHQ or AFRQ allele[7] from human consumption (subject to a negative test for animals over 18 months).

5- Conclusions and opinion

On the following grounds:

- the discriminatory tests do not enable the presence of BSE to be ruled out either in the tested animal or by extension in the flock to which it belongs;
- the transmission to humans of TSE strains other than BSE cannot be ruled out;
- the knowledge acquired of the genetic susceptibility of sheep to scrapie and BSE should be used, insofar as this is possible, to limit the risk of consumer exposure,

The Committee is making the following recommendations:

Recommendations common to both types of control measure:

- permanent individual identification of all small ruminants belonging to the herds concerned.
- for sheep, genotyping for the four cordons (136, 141, 154 and 171) of all animals in an infected flock.
- all tests carried out on animals slaughtered or culled as part of the control measures must be effected with one of the rapid tests with the best sensitivity for the detection of atypical scrapie (currently Idexx, Biorad).
- conduct of a discriminatory test on all secondary cases identified.
- destruction of all positive animals.

Control measures on goat or sheep farms where a case of classical scrapie has been detected

The Committee recommends that the current control measures should be maintained, since the Commission's other two proposals incur an additional risk from the consumption of animals carrying a susceptible genotype and could release for consumption tissue containing large quantities of the infectious agent despite a negative rapid test.
In the event of the detection of a case of atypical scrapie in one of the secondary cases, animals with a ARR/AHQ or ALRR/AFRQ genotype should not be released for human consumption for a period of 5 years (minority view: this measure should not be applied).

Control measures on goat or sheep farms where a case of atypical scrapie has been detected

Whilst awaiting new scientific data, the Committee recommends:

- putting in place surveillance for a 5-year period in herds infected with atypical scrapie;
- the destruction at the end of their economically useful life of animals carrying AHQ and AFRQ alleles from these herds (minority view: this measure should not be applied);
- a ban on the sale of breeding stock to farms with a different status;
- all animals from infected herds slaughtered or culled and aged over 18 months should be tested using one of the rapid tests most suitable for the detection of atypical cases (currently the Biorad and Iddex tests);
- in the event of the detection of classical scrapie in one of these secondary cases, the corresponding control measures should be applied, and animals with the genotype

[7] Given i) the low prevalence of secondary cases in outbreaks of atypical scrapie; ii) the additional risk, consequently estimated as low, that an animal with one of the most susceptible genotypes would develop the disease; iii) the lack, to date, of any evidence of PrPres and infectivity outside the central nervous system, the SRM removal measures appear sufficient to limit consumer risk as far as is possible.

ARR/AHQ or ALRR/AFRQ should not be released for human consumption for a period of 5 years (minority view: this measure should not be applied).

6- Responses to the specific questions posed by DGAl and AFSSA

1) *Does the CES consider that products from sheep and goats from flocks infected with classical scrapie, slaughtered in the conditions described above, represent an additional risk to public health compared with products from genetically resistant sheep only?*

The data contained in paragraph 3 of this opinion illustrate the additional risk of infection from individuals with a "susceptible genotype" born in a herd infected with classical scrapie. The Committee has also, on several occasions, stated that a negative result from a screening test conducted on a brain tissue sample from an animal over 18 months old is not a guarantee of the absence of infectivity from this animal's tissue. This is particularly true in animals of a susceptible genotype in which the secondary lymphoid organs generally contain high quantities of the infectious agent.
Consequently, the Committee unequivocally considers that products obtained from sheep and goats from herds infected with classical scrapie, slaughtered under the conditions defined in the document presented by the Commission, represent an additional risk to public health compared with products from genetically resistant sheep only.

2) *In the knowledge that the current surveillance tools for small ruminants at best enable the detection of only a fraction of the flocks infected with a TSE and that the sheep population is composed in part of genetically susceptible animals, can the CES compare the above-mentioned risks with the risk from an "ordinary" animal slaughtered under the conditions currently in force?*

A relevant quantitative assessment of these risks is currently impossible due to insufficient data on:

(i) the actual prevalence of scrapie in all infected herds;
(ii) the actual genetic structure of the sheep population in general (besides the distribution in the breeding population).

However, the data quoted in this opinion on the prevalences observed in certain flocks infected with classical scrapie enable a rough evaluation of this additional risk if one considers that:

- the prevalence of classical scrapie in the general population of slaughtered animals aged over 18 months is of the order of 0.05%;
- the prevalence in flocks infected with classical scrapie can vary by between approximately 1 and 30% (without taking account of individual genotypes). Therefore, the relative risk represented by an animal from an infected flock compared with an animal from the general population is 20 to 600. This additional risk is increased again if one considers solely the animals with a susceptible genotype from the infected flocks.

3) *What measures, in particular as regards the removal of specified risk material or BSE tests, could be recommended to reduce any additional risk which might be identified above?*

Complete removal of the intestines, whatever the age of the individual, would improve the level of guarantee provided by SRM removal. However, as the Committee has stated on numerous occasions[8], with small ruminants, no system based solely on SRM removal can provide the same level of safety as it does for cattle.

[8] Afssa Framework opinion of 25 March 2005 on the analysis of the risks from transmissible spongiform encephalopathies in the small ruminant sectors, the strengths and weaknesses of the current system and the options for change. Update of the February 2002 Opinion
Afssa opinion of 20 July 2006 on assessment of the risk from the potential presence of BSE in sheep on 20 July 2006

In terms of tests, in view of the dissemination pattern and kinetics of the BSE agent or the agents responsible for classical scrapie in small ruminants, lowering the age of animals tested on a sample of obex to 12 months could enable the identification of more cases without, however, having much effect on the system effectiveness. Only by testing samples of both the obex and of the lymphoid tissues (tonsils, mesenteric lymph nodes) will the desired objectives be achieved.

However, very few of the tests validated by the European Commission have been on samples of this type[9] and the conditions for use of these tests, in routine practice, have not been established.
The Committee is therefore unable to suggest any immediately operational means of reducing the additional risk from the consumption of sheep carrying a susceptible genotype in an infected flock.

4) *Based on the answers to the preceding questions, could you carry out a comparative analysis of the potential level of risk represented by the eradication strategy as compared with the alternative strategy as regards the animal health and public health issues.*

The Committee considers, unequivocally, that the strategies proposed as an alternative to the eradication strategy present a significant additional risk in terms of both public and animal health. In view of the deadlines imposed, and the data currently available, a comparative, quantified and relevant analysis is impossible.

5) *Finally, with a view to permitting the consumption of animals from herds with a TSE outbreak, would it be pertinent to lower the age at which animals are tested, currently suggested as 18 months by the Commission?*

The answer to this question is included in the answer to question No. 3.

Subsidiary questions:

- strain typing can only be carried out on index cases;
The Committee has clearly stated its view on the necessity of conducting a discriminatory test on the index case and all the secondary cases in a herd.

- a surveillance period should be 3 years instead of 2;
In the case of classical scrapie, the Committee would like to see the continuation of the current control measures which require surveillance for a 3-year period. In the case of atypical scrapie, it would like to see surveillance for 5 years.

- tests on animals over 18 months could be done by sampling;
As regards the public health objective, it would mean not testing all animals intended for consumption and would therefore permit the consumption of positive animals from these herds including some at a late stage of incubation. In terms of a knowledge improvement objective, it would dramatically affect estimation of the prevalence of these outbreaks, in view of the very low prevalence observed from the data available.
Consequently, the committee is not recommending this option.

- SRM removal could be extended to the complete head and all the intestines;
See answer to question No. 3

[9] Scientific Report of the European Food Safety Authority on the Evaluation of Rapid *post mortem* TSE Tests intended for Small Ruminants. Question N° EFSA-Q-2003-084. Adopted on 17 May 2005 and on 26 September 2005.

- finally, products from these animals would be restricted to the national markets
The Committee considers that the European Commission's proposal to permit the consumption of animals tested negative solely in the Member State in which a given outbreak has been detected has no rational basis in terms of public health protection, if the objective is a homogenous management of this aspect at European level. The Committee would also like to point out the difficulties inherent in controlling flows of animals and products in the absence of a permanent system of individual identification for small ruminants at European level.

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