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OPINION

of the French Food Safety Agency (Afssa) regarding the revision of conditions for use of meat and bone meal in animal feed

DIRECTOR GENERAL

Reminder of the request:

In a letter dated 9 April 2008, Afssa asked its TSE Expert Panel to revise the conditions for use of meat and bone meals in animal feed.

The terms of the internal request were as follows:

“For the management of the BSE crisis, restriction and control measures that were part of an overall approach to the eradication of the disease were implemented on the national and EU level. These included:

- *the implementation of a list of specified risk material (SRM);*
- *a ban on the use of meat and bone meal (MBM) in livestock feed;*
- *the establishment of active TSE monitoring based on the use of rapid screening tests.*

In July 2005, in view of the improved situation (particularly the decrease in the number of cases of BSE), the European Commission published a roadmap proposing a change in some restrictive measures. As regards the ban on meat and bone meal, the roadmap envisages lifting the current ban, subject to the fulfilment of certain conditions (preliminary evaluation of the risk and validation of tests enabling differentiation of animal proteins from certain species). In keeping with the ban on intra-species recycling provided by (EC) regulation 1774/2002, the ban on using MBM in ruminant feed would remain in effect, pigs, for example, could be fed with poultry MBM and vice versa.

In July 2007¹, Afssa issued an opinion concerning assessment of the effectiveness of the measures taken to control the BSE risk. In view of the epidemiological situation in France, the opinion proposed a change in some measures such as the reduction of the list of SRMs and less stringent screening of younger animals. However, the opinion recommended the maintenance of measures intended to prevent the agents responsible for BSE from circulating within animal populations once again. As a result, the Panel recommended the maintenance of the ban on the use of animal meal in livestock feed.

At the same time, in its opinion of 17 October 2007, the EFSA specified that, based on the current state of scientific knowledge, there was no risk of transmission of BSE to pigs and poultry. However, it stressed that the existence of test methods to quantify and specify the original species present in the MBM was a prerequisite for the possible reintroduction of MBM in feed for pigs and poultry, and for the definition of a tolerance limit for the presence of such MBM.

The Commission has initiated a European research programme named “SAFEED PAP”, which should make it possible to develop these test methods, the results of which are expected in 2009.

In recent months, mainly because of the sharp increase in the price of grain, feed manufacturers have expressed their desire that the possibility of using animal meal be examined once again.”

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¹ Afssa opinion dated 17 July 2007 assessing the effectiveness of the measures taken in November 2000 to control the BSE epizootic.

Afssa has requested the TSE Expert Panel to evaluate the appropriateness, with regard to health risks, of reintroducing animal meal into non-ruminant feed while maintaining the ban on intra-species recycling. The Panel was specifically asked to base its assessment on the current epidemiological situation as well as on the organisation of animal feed manufacturing processes.

Expert assessment method:

The TSE Expert Panel, assisted by the working group on the epidemiology of animal TSE, issued the following opinion on 9 December 2008.

The expert assessment was based on:

- Current scientific knowledge about the transmission of TSEs to non-ruminant livestock, namely pigs and poultry;
- The lessons drawn from epidemiology studies of the control of the BSE risk in France;
- Scientific data about the identification of the species from which the animal protein in Processed Animal Proteins (PAPs) is derived;
- The organisation of animal feed manufacturing processes, based on documents supplied by the DGAI (General directorate for food).

Scientific arguments:

1. Definition of MBM and manufacturing conditions

The term MBM, standing for meat and bone meal, has been replaced by PAPs or Processed Animal Proteins since (EC) regulation 1774/2002 (relating to by-products) and this same terminology will be used in this opinion.

According to (EC) regulation 1774/2002, processed animal proteins are defined as “*animal proteins derived entirely from Category 3 material, and which have been treated (in compliance with the provisions in annex V, section II) so as to render them suitable for direct use as feed material or for other use in feedingstuffs, including petfood, or for use in organic fertilizers or soil improvers; it does not include blood products, milk, milk-based products, colostrum, gelatin, hydrolysed proteins and dicalcium or tricalcium phosphate, eggs and egg products, tricalcium phosphate or collagen*”.

It must be stressed that processed proteins from mammals “*must be processed using processing method 1 (maximum particle size 50 millimetres, core temperature above 133 °C for at least 20 minutes without interruption and at a pressure (absolute) of at least 3 bars produced by saturated steam. PAPs that are not derived from mammals may be processed using other methods (methods 1 to 5 and 7 of section III of annex V of (CE) regulation 1774/2002)*”.

Category 3 material is defined in article 6 of (CE) regulation 1774/2002. This material mainly consists of “*parts of slaughtered animals, which are fit for human consumption in accordance with Community legislation, but are not intended for human consumption for commercial reasons*”, and also “*parts of slaughtered animals, which are rejected as unfit for human consumption but are not affected by any signs of diseases communicable to humans or animals and derive from carcasses that are fit for human consumption in accordance with Community legislation*”.

This means that category 3 materials that may be used to produce PAPs are highly varied in nature.

2. Current scientific knowledge of TSE transmission to non-ruminant livestock – pigs and poultry

Some experimental studies have shown that pigs can be infected by the BSE agent and develop a TSE when the infectious agent is administered to them parenterally (Dawson *et al.*

1990; Ryder S.J *et al.* 2000). On the other hand, the species seems resistant to the BSE agent by the oral route, as suggested by a study on pigs fed several times with brain samples containing fairly high infectious loads (Wells *et al.* 2003). However, since the number of experimental transmission tests is quite limited, the degree of certainty about the resistance of pigs to the BSE agent by the oral route needs to be weighted.

Similarly, no transmission of the BSE agent to poultry has been demonstrated until now although a few experimental tests have been performed (Cawthorne *et al.* 1997, Matthews *et al.* 1990).

In the current state of scientific knowledge, it seems that there is a species barrier by the alimentary route protecting pigs and poultry from ruminant TSEs (which is liable to limit the propagation of TSE agents within these species by recycling).

However, in view of the lessons drawn from the mad cow disease crisis with regard to the risks of feeding an animal species with PAPs from that same species, the principle of cannibalism avoidance remains appropriate.

3. Lessons drawn from epidemiology studies of the control of the BSE risk in France

The authorisation to use PAPs manufactured from category 3 poultry materials for feeding pigs and *vice versa* raises a certain number of questions related to the risk of cross contamination in mixed farms where pigs and poultry are reared, and in which ruminants are found as well.

That is why the animal TSE epidemiology working group has identified several studies that provide an overall understanding of the sources of infection by BSE of the bovine population in France after the ban on PAPs in cattle feed in 1990 (see report in Annex).

The first conclusion is that the ban on PAPs in cattle feed in 1990 alone did not totally eliminate the sources of contamination. The main source of infection in cattle born after 1990 seems related to cross contamination of their feed, mostly in the industries manufacturing cattle feed, and to a lesser degree in farms (cross contamination of feed with feed that could still legally contain PAPs – feed for sheep up to 1994, feed for poultry and pigs up to 2000).

That is why, due to a lack of the separation of processes and the imperfect application of the regulations, cattle continued to be exposed to contaminated ruminant PAPs after 1990.

If the use of poultry PAPs were once again allowed in pig feed or if the use of pig PAPs were allowed once again in poultry feed, the health risks associated with such a move would be the following, through cross contamination:

- the PAPs used to make feed for monogastric animals could be contaminated with raw material from ruminants during the processing stage or when they are incorporated into compound feeds; and thus, the PAPs used in the feedstuffs for monogastric animals could be distributed to ruminants in farms, or
- proteins could be recycled within the same species, that is PAPs derived from pigs incorporated into pig feed and poultry PAPs incorporated into poultry feed (which would be considered animal cannibalism and is banned under Community regulations²).

These risks could be contained by:

- separating the raw materials and processed products by species at every stage of manufacturing;
- using inspection methods to identify the animal species from which the PAPs are derived in order to verify the enforcement of such separation.

² (EC) regulation 1774/2002

4. Methods for the identification of the animal species from which processed animal proteins are derived

In its opinion of 17 October 2007, the EFSA stressed that the existence of methods to verify the animal species from which PAPs are made is an indispensable prerequisite for the possible lifting of the ban on the use of certain PAPs from non-ruminant species in feedstuffs for monogastric animals.

European Directive (EC) 126/2003 sets out the first method for detecting the origin of PAPs. This method relies on the macroscopic detection of bone fragments and morphological identification that makes it possible to distinguish between fragments from mammals, poultry and fish (Lai *et al.* 2008). The approach does not however enable the identification of the mammal species (cattle, pigs, sheep or goats) from which the PAPs are made. The lifting of the ban on animal meal would make it necessary to demonstrate the specific absence of material from ruminants, in addition to identifying the species of origin.

To achieve this aim, two approaches based on the detection of nucleic material or protein material respectively are being considered by the European Commission:

Detection of protein material

These methods rely on the detection of antigens of the processed animal proteins. Commercial methods are already available that can specifically differentiate ruminant proteins from those of other species (Myers *et al.* 2005) but have not been validated to date. The detection limit for such methods is thought to be close to 1% (Myers *et al.* 2007). However, heat treatment might denature the proteins, making them more difficult to detect.

Detection of nucleic material (DNA)

These methods rely on detection in the PAPs of nucleic acid genome sequences that are specific to a given species (Lahiff *et al.* 2001). The most efficient of such tests rely on a method of quantitative amplification (QPCR). The material is detected after extraction of nucleic acids with probes specific to each species. This makes it possible to identify the animal origin of the product. The species tested include cattle, pigs, goats and sheep. In these tests, the specificity of the amplifications and their detection limits are crucial. In a recent study comparing the results obtained in three laboratories (Prado *et al.* 2007), the tests were capable of detecting 0.1% of cattle-based material in different meal mixtures. However, this detection method can lead to false positives under certain conditions because it cannot discern authorised by-products from banned ones within the same species (traces of DNA found in animal fat or other authorised products).

Detection limit of the techniques / tolerance limit

The definition of a tolerance limit for the presence of PAPs in feed for livestock has been touched upon by the Commission in its TSE roadmap.

The EFSA has stressed that even with a PAP incorporation rate of 0.1% in feed for ruminants, the risk of transmission of a TSE agent cannot be ruled out. Because each method is limited by a PAP detection limit, traces of such banned proteins could potentially still be found in livestock feed.

The definition of a maximum PAP level in feed where the risk of transmission of a TSE is considered to be negligible is not currently possible. That definition depends on several insufficiently documented parameters - the minimum infectious dose of contaminated PAP for each species in question, combined with the sensitivity of the tests for detecting the PAP from each species within a mixture.

No currently validated method exists that could thus be applied in the field.

5. The organisation of animal feed production processes

The Panel has stressed the essential role of maintaining control over the circuits at all stages (choice of raw materials, processing conditions, transport conditions, receiver animal production plants) to minimise the risk of the re-circulation of TSE agents in susceptible animals.

The implications of a partial lifting of the ban on PAPs for non-ruminant species in respect of the various stages of the current livestock feed manufacturing process are many:

Collection and processing

The separation of the by-products by species in high production zones where slaughtering lines or even slaughterhouses are specialised, appears possible. On the other hand, in multi-species abattoirs where relatively small numbers of animals are slaughtered, separate collection would probably be difficult to achieve. The same applies to collection from butchers and in cutting facilities handling meats of different species of livestock, and the collection of foodstuffs with expired freshness dates from sites where they are sold to consumers.

Here are a few examples of the tonnages of PAPs that are currently produced. According to the data supplied by SIFCO³, 5% of the PAPs were used in 2007 for the production of animal and fish feed and 30% to make pet food, the remainder being used to produce energy. Four categories can be identified on the basis of their origin:

- Multi-species PAPs including ruminants (45%)
- Poultry PAPs/feather meal (34%)
- Pig or Pig/poultry PAPs (16%)
- Blood/blood product PAPs (5%)

In its data, SIFCO does not differentiate pig PAPs from poultry PAPs except in the category poultry PAPs/feather meal.

In order to consider the use of PAPs as livestock feed, the conditions that would offer the guarantee of the exclusive use of raw materials from either poultry or pigs need to be defined.

Production of compound feed and transport

Most of the feed for poultry and pigs is manufactured in compound feed factories that produce more than 100,000 tonnes per year. Most of these factories are not specialised by species (plants process both pigs and poultry); in other words, compound feed is made using the same machinery – silos, crushers, mixers and presses.

As regards transport, the same lorries often deliver feed for both pigs and poultry, often within a single delivery round.

In order to consider the use of PAPs for these species, measures must be defined to make sure that there is no cross-contamination during manufacturing and transport, whether through the use of separate manufacturing lines or means of transport for each species or through validated cleaning procedures.

³ Union of French industries of animal by-products, which represents 72 production units (approximately 2.8 million tonnes of raw material, of which 72% is category 3)

Use in farms:

The PAP use issue depends on the size and specialisation levels of the farms.

In intensive production farms, where feed is delivered in bulk, the animals are reared in specialised buildings equipped with silos. In view of the specific nature of these installations, the likelihood of distributing feed intended for other species is limited, even if several livestock species co-exist in the farm.

Nevertheless, feed is made on the farm in close to a third of pig farms. Grain and possibly protein seeds (peas, horse beans) or oil seeds (sunflower, rape) are produced in the farm and mixed by the breeders with a food supplement sourced from outside that provides proteins, minerals, trace elements and vitamins. The supplement may be used for other livestock species present in small numbers in mixed farms. In the poultry sector, feed is made on-site in only a minority of farms.

In general, in small-scale farms where several species are reared together in limited numbers, the feed purchased from outside may be delivered in bags. In that case, an error, negligence or procurement shortage may mean that the feed is not necessarily given to the species for which it is intended.

It is also important to stress that due to the very limited number of official inspections (5% of farms every year on average), farmers are responsible for controlling the traceability of feed in order to avoid cross-contamination.

Lastly, it must also be noted that PAPs intended to be used as fertilising material and agricultural aids and stored in farms rearing livestock may be mixed accidentally or fraudulently to animal feed. Such PAPs, which are used as fertilisers, are derived from category 2 materials from different species (including ruminants) and do not meet the same criteria as those that are allowed for feeding monogastric animals. For this reason, it is crucial that these PAPs be rendered unpalatable, which is not the case at present.

Conclusions of the TSSE Expert Panel

In view of currently available knowledge, the Panel considers that the use of avian PAPs for feeding pigs or pig PAPs for feeding poultry is not in itself likely to contribute to the propagation of TSEs.

However, if such a measure is envisaged, the Panel believes that the preparation processes for single-species PAPs must be made absolutely watertight to prevent intra-species recycling of infectious agents.

These processes ought to also be watertight with regard to materials from sheep, goats and cattle, because the contamination of single-species PAPs by such raw materials is likely to lead to the recycling of the agents of a TSE in ruminants if the PAPs are used accidentally or fraudulently in their feed. Further, such separation would also make it possible to prevent the risk of the adaptation of new strains of TSEs to pigs and to a lesser extent to poultry, even though no scientific data is currently available demonstrating the sensitivity of these species to TSE agents by the oral route.

In addition, the use of poultry PAPs for pig feed and vice versa will depend on the availability of a validated method for identifying the contaminants of single-species PAPs. The Panel believes that it is thus not possible to envisage the use of PAPs to feed poultry or pigs at the present time. If validated identification methods were to become available, the ban on the use of PAPs for feeding pigs and poultry could be lifted along with the establishment of a monitoring system for the collection of raw materials intended for the manufacturing of PAPs that incorporates the traceability of the material up to the plants that manufacture pig or poultry feed. Complete traceability of the use of the PAPs in plants manufacturing livestock feed should also be implemented in order to guarantee the absence of cross-contamination (pig/poultry) and the absence of incorporation in other cattle feed.

Lastly, the difficulty in controlling cross-contamination in farms would probably lead to limiting the use of such feed only to farms that are specialised in single production (pigs or poultry).

Opinion of Afssa

To conclude, it would appear that the lifting of the ban on the use of poultry PAPs for pig feed and pig PAPs for poultry feed depends on the following:

- 1) the existence of a validated method for detecting and identifying processed animal protein depending on the species.
- 2) the complete separation of the processes producing such processed animal protein.
- 3) means for controlling and tracing the processes.

Because these conditions are not yet fulfilled, Afssa recommends the maintenance of the current measures relating to the ban on the use of processed animal protein in livestock feed.

6. References:

Opinion of Afssa of 17 July 2007 assessing the effectiveness of the measures taken in November 2000 to control the BSE epidemic.

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Commission Directive 2003/126/EC of 23 December 2003 on the analytical method for the determination of constituents of animal origin for the official control of feedingstuffs.

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Opinion of the Scientific Panel on Biological Hazards of the European Food Safety Authority on the "Quantitative risk assessment of the animal BSE risk posed by meat and bone meal with respect to the residual BSE risk". (Question N° EFSA-Q-2003-099).

Prado M, Berben G, Fumière O, van Duijn G, Mensinga-Kruize J, Reaney S, Boix A, von Holst C. *J Agric Food Chem.* 2007 Sep 5;55(18):7495-501. Detection of ruminant meat and bone meals in animal feed by real-time polymerase chain reaction: result of an interlaboratory study.

Regulation (EC) 1774/2002 of the European Parliament and of the Council of 3 October 2002 laying down health rules concerning animal by-products not intended for human consumption.

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Keywords: meat and bone meal, processed animal protein, PAPs, TSE, animal feed, feedingstuff.

Annex

Report of the Animal TSE epidemiology working group on the reintroduction of processed animal protein in animal feed

Background

On 9 April 2008, Afssa referred the matter to its TSE Expert Panel of the appropriateness with regard to health of the reintroduction of animal meal in feed for non-ruminants, with a continuing ban on inter-species recycling.. This assessment was to be based both on the current epidemiological situation and also on the organisation of the processes used in the production of feed intended for animals.

As part of this expert assessment, the TSE Expert Panel turned to the Animal TSE epidemiology working group for an appraisal of the management of BSE risks in France from 1990 to 2000. This report is the result of the discussions of the working group on 14 May 2008.

Lessons drawn from epidemiology studies of the management of BSE risk in France

BSE control measures were first implemented in France at the start of the 1990s¹, and several studies have been carried out in recent years that throw some light on the way in which the risk of BSE has been managed in France since that time.

A case-control study was carried out to determine the factors relating to contamination in BSE cases arising between 1990 and 1996. The main risk factor was related to cattle feed, which was in principle made safe since 1990 by placing a ban on the incorporation of meat and bone meal (MBM). Additionally, the presence of poultry on the farms also increased the risk of contamination, indicating a possibility of cross-contamination in mixed farms. A third risk relating to milk replacements was also highlighted, but the farms using purchased feed for cattle also very often used milk replacements².

A case study was conducted to determine the factors relating to contamination in BSE cases in animals born after 1996. That study was conducted based on the investigations of the national veterinary and plant-protection investigation brigade of the Directorate General of Food (DGAI). The risk relating to meal could not be ruled out in any of these investigations, since meal was still being used in the industries that supplied feed to the farms in question. The investigations carried out with manufacturers indicated that the control measures for preventing cross-contamination of feed for cattle by MBM were generally not implemented or implemented very partially. On the other hand, in most cases, other factors such as the risk relating to MBM imported by the manufacturers who had supplied feed to infected farms, cross-contamination occurring on the farm and transmission by milk replacements and maternal transmission could be ruled out³.

A geographical study of the distribution of BSE cases in animals born after the measures of 1990 (known in French as "NAIF", born after the animal meal ban in bovine feed) and 1996 (known as "SuperNAIF", born after removal of SRM from animal meal) has shown that

¹ Main control measures put in place successively in France.

July 1990: meat and bone meal (MBM) other than that from milk, eggs and fish was banned in cattle feed

December 1994: MBM other than that from milk, eggs and fish was banned from the feed intended for all ruminants.

June 1996: setting up of a system to make MBM safe. Removal of specified risk material (SRM) from the human and animal food chain and destruction by incineration; systematic destruction by incineration of carcasses of animals of all species and health seizures; reinforced heat treatment – 133°C-20 min-3 bars-50-mm particles – for proteins from mammals intended to be used as feed for poultry, pigs and fish.

November 2000: suspension of the use of MBM and some fat in feedstuffs for all animal species providing products intended for human consumption

² Jarrige, N., C. Ducrot, et al. (2007). "Case-control study on feed risk factors for BSE cases born after the feed ban in France." *Vet Res* **38**: 505-516.

³ Jarrige, N., C. Ducrot, et al. (2006). "Potential sources of infection for BSE cases born in France after 1996." *Vet Rec* **159**: 285-286.

the BSE risk was heterogeneous over time, and the zones that were most at risk for SuperNAIF cases were adjacent to zones that were most at risk for birth cohorts born immediately before these SuperNAIF cases, which suggests a common cause of infection⁴. This study supports the study carried out earlier on the space and time distribution of BSE cases⁵.

A spatial analysis of the 380 NAIF BSE cases detected from July 2001 to December 2003 in France was carried out and compared with pig density (all breeding methods taken together) and poultry density (all breeding methods taken together)⁶. The major finding of the study was that the BSE risk is statistically related to pig density on the national level and linked simultaneously to pig density and poultry density on the local level. The results obtained seem to support the hypothesis of cross-contamination between feed for monogastric animals and cattle feed as the source of contamination of NAIF cases in France.

Lastly, a recent article that has not yet been published⁷ provides information explaining that in spite of the regulations, manufacturers did not immediately implement process separation measures due to structural and production constraints.

The lessons that have been drawn from these different studies may be summarised as follows⁸:

"... different epidemiology studies have been carried out in a complementary manner on the sources of infection of cattle by BSE. They were based on various sources of information using different test methodologies and have produced convergent results that make it possible to have an overall understanding of the sources of infection by BSE in the bovine population in France after the ban on MBM in cattle feed in 1990.

The first lesson is that simply banning the administration of MBM to cattle did not totally eliminate the sources of infection. With the passing of time and data from several other European countries, this analysis is shared by the experts in the field. The implementation of such a ban implies sweeping changes in the manufacturing processes and does not remove all the sources of cross-contamination. There must be no mistake – the aim is not to claim that the measure is insufficient for controlling a BSE epidemic like the one experienced in Europe. A control measure, even an imperfect one, can be enough to gradually control a disease if it succeeds in driving the rate of transmission of the disease in the population concerned below a limit that makes the disease eventually unsustainable.

The second lesson is that the main source of infection in cattle born after 1990 was related to the imperfect implementation of the control of the composition of cattle feed by the feed industry. Cattle contamination through the use in farms of feed materials that could lawfully contain MBM – poultry feed in particular – appears in retrospect to have played only a secondary role.

The third lesson is that the cases of BSE detected in France seem to be linked to feed causes. Epidemiology studies have shown that there is continuity in the feed risk over time and space, and that the factors of the risk of infection are stable. This analysis is borne out by studies into the risk of BSE infection in relation to birth cohorts, which demonstrate that the risk was considerably reduced since the mid 1990s and was close to nil at the end of the 1990s."

⁴ Abrial, D., D. Calavas, et al. (2005). "Spatial heterogeneity of the risk of BSE in France following the ban of meat and bone meal in cattle feed." *Prev Vet Med* **67**(1): 69-82.

⁵ Ducrot, C., D. Abrial, et al. (2005). "A spatio-temporal analysis of BSE cases born before and after the reinforced feed ban in France." *Vet Res* **36**: 839-853.

⁶ Abrial, D., D. Calavas, et al. (2005). "Poultry, pig and the risk of BSE following the feed ban in France - Spatial analysis." *Vet Res* **36**: 615-628.

⁷ Persistence of 'mad cow disease' in France despite control measures: a geographical approach, Paul, M., Salem, G., Abrial, D., Rican, S., Calavas, D., Ducrot, C, submitted.

⁸ Jarrige, N., D. Abrial, et al. (2007). "L'E.S.B. en France après l'interdiction des farines animales dans l'alimentation des bovins." *Le Nouveau Praticien Vétérinaire élevages et santé* **9**: 9-15.