ADVISORY COMMITTEE ON THE MICROBIOLOGICAL SAFETY OF FOOD

RISK ASSESSMENT: THE POSSIBLE HEALTH RISKS TO CONSUMERS ASSOCIATED WITH *M. BOVIS* AND UNPASTEURISED MILK AND MILK PRODUCTS (v.1 Sept 2011)

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1.0 Statement of purpose

The purpose of this risk assessment is:

- To assess the potential for **unpasteurised milk and milk products** contaminated with *Mycobacterium bovis* to enter the food chain
- To assess the risk to consumers associated with these products
- To assess whether the risk has changed in light of the increase in *M. bovis* infection in cattle in the UK

Background

1. In its 2002 Report on *M. bovis*, the ACMSF concluded that there were no concerns in relation to milk and dairy products as the exposure pathway seemed well protected by the existing legislation and controls.
2. In autumn 2009, the FSA Board requested that the Agency review the potential risks to consumers of meat and milk from cattle with *M. bovis* infection as the incidence o*f M. bovis* infection in the UK cattle population has increased since the ACMSF last considered the issue in 2001.
3. Consequently, in March 2010 the ACMSF reviewed changes in the hygiene regulations and disease incidence in cattle and humans which have taken place over the last 10 years. The Committee confirmed the result of its earlier 2001 risk assessment on meat and concluded that the risk remained very low.
4. In September 2010 the Committee assessed the potential for pasteurised milk and milk products contaminated with *M. bovis* to enter the food chain and whether the risk has changed in light of the increase in *M. bovis* infection in cattle in the UK. Their conclusion was that the risk from pasteurised milk and milk products contaminated with *M. bovis* has changed but in milk that is properly pasteurised the risk remains acceptably low.
5. The results of the meat risk assessment were reported back to the FSA Board in July 2010 and a further report is planned in autumn 2011, following completion of the risk assessments on pasteurised and unpasteurised milk and milk products.

2.0 Hazard Identification *(A description of the nature of the hazard e.g. microorganism/toxin capable of causing adverse health effects and the food of concern)*

6. The hazard is the bacterium *M. bovis* in unpasteurised milk and milk products produced in the UK.

7. *M. bovis* is the causative agent of bovine tuberculosis. It is capable of infecting a wide-range of warm blooded animals including humans and has also been found in other farmed livestock, wildlife, domestic cats and dogs. In humans infection with *M. bovis* causes a disease very similar to infection with *M. tuberculosis*, which is the primary agent of tuberculosis in humans.[1]

8. *M. bovis* infection can be spread to humans by eating or drinking contaminated foodstuffs, by inhalation of airborne droplets of moisture (aerosols) containing the organism from infected animals or carcases and, more rarely, through contamination of skin wounds. Prior to the widespread adoption of pasteurisation in the mid-20th century *M. bovis* contaminated milk was an important cause of childhood tuberculosis in the UK.[2]

9. This risk assessment is concerned with *M. bovis* in unpasteurised milk and unpasteurised milk products produced in the UK. Unpasteurised milk is milk which has not been pasteurised (72°C for 15 seconds) and is sometimes referred to as raw drinking milk. Unpasteurised milk products (e.g. cheeses, cream, butter, yogurt) are those made with milk which has not been pasteurised. This risk assessment encompasses unpasteurised milk and milk products from any species farmed for its milk e.g. cows, sheep, goats and buffaloes.

10. Other hazards in unpasteurised milk and milk products may include *E.coli* O157, *Salmonella* spp., *Campylobacter* spp. and *Listeria* spp., which are outside the scope of this risk assessment.

3.0 Hazard Characterisation *(A description of the potential adverse health effects attributable to the specific hazard, the mechanisms by which it exerts its effects, and the associated dose-response relationship.)*

11. Human tuberculosis can be caused by several mycobacterial species including *M. bovis* and *M. tuberculosis.* Human tuberculosis due to *M. bovis* is clinically indistinguishable from tuberculosis caused by *M. tuberculosis*. *M. tuberculosis*, the most common cause of human tuberculosis in the UK is most frequently contracted through person-to-person airborne transmission. Although infection usually involves the lungs (pulmonary tuberculosis) mycobacteria can attack a number of organs in humans.

12. Tuberculosis in immunocompetent individuals is characterised by a slowly developing chronic infection after a long incubation period. Symptoms which can persist for months or years depend on the organ(s) infected. For example the symptoms of intestinal tuberculosis (which can results from direct ingestion of the organism) include fever, chills weight loss, abdominal pain, diarrhoea or constipation.

13. Infected immunocompetent individuals may not initially display symptoms as their immune systems can control infection (latent tuberculosis). However if they subsequently become immunocompromised, persistent mycobacteria may reactivate causing secondary/post-primary/reactivation tuberculosis. Intestinal TB can occur after reactivation of primary infection.

14. In the absence of immunosupression, person to person transmission of tuberculosis caused by *M. bovis* is rare [3,4,].

15. The Bacillus Calmette-Guérin (BCG) vaccine is regarded as being 70 – 80% effective at preventing disease due to *M. tuberculosis* and is suggested to be equally effective against *M. bovis*[5]. Most UK adults will have been vaccinated under a universal school vaccination programme introduced in 1953. However, since 2005 vaccination is now only offered to babies in areas with high rates of TB or babies whose parents or grandparents were born in a country with a high prevalence of TB. A UK study indicated that BCG-mediated protection lasts 10 to 15 years after vaccination[6].

16. Children are generally at greatest risk of infection and the highest rate of cases of TB (20.8 per 100,000) due to *M. tuberculosis* occur amongst individuals aged 15-44 years. The immunosuppressed and very young infants are most at risk of acute primary infection (miliary tuberculosis). By contrast, human *M. bovis* infections in the UK are most commonly diagnosed in individuals aged over 65 years.

17. The reported tuberculosis mortality rate in England and Wales in 2008 was 0.6 per 100,000 population[7]. The specific mortality

rate for human tuberculosis caused by *M. bovis* is unknown.

Dose-response relationship

18. No reports are available on human dose response following ingestion of *M. bovis* but extrapolation from animal studies (on sheep, cattle and guinea pigs) suggest that the human infectious dose of *M. bovis* by the gastrointestinal route is in the region of millions of organisms.

19. Infection via the oral route requires thousands (10^3) or millions (10^6) more organisms than infection via the inhalation route. For example pulmonary infection in guinea-pigs required 1 to 62 (10^1) organisms whereas infection by the oral route required 16-18 million more organisms (10^7)[8].

20. A bovine model of infection developed for vaccine and diagnostic studies[9] showed that for the respiratory route challenge with 10^3 - 10^4 colony forming units of *M. bovis* generated the same symptoms as the natural disease, whereas challenge with higher doses (10^5 - 10^6 cfu) produced atypical lesions.

21. Approximately 10% of human infections will develop to active tuberculosis within the individual's lifetime, with around 50% of these showing symptoms within two years. HIV infection is the most significant risk-factor leading to reactivation of latent tuberculosis with 5-8% of TB/HIV co-infected individuals annually displaying reactivation[10].

22. The infectious dose for vulnerable groups (very young and immunocompromised) is unknown. It could be the same as for the general population and is likely to be considerably less.

23. The effects of different food matrices on infectious dose are unknown.

Incidence and outbreaks

24. The HPA and its partner agencies across the UK have carried out a national surveillance programme for TB in humans since 1994[11]. Over that time, despite an increase in the incidence of TB in cattle, only a very small proportion of reported human TB cases each year in the UK were due to *M. bovis,* the vast majority of human infections have continued to be caused by *M. tuberculosis.* In 2009 25 or 0.5% of culture confirmed cases of tuberculosis in the UK were identified as due to *M. bovis*, a figure

that has remained relatively stable in recent years[11].

25. Most human cases due to *M. bovis* occur in people born in the UK before 1960, suggesting reactivation of old infection that was acquired when the prevalence of *M. bovis* in the UK cattle population was higher and when pasteurisation of milk and cattle testing programmes were not so widespread. About 20% of cases occur in non-UK born persons (suggesting infection contracted abroad). A very small number of human cases have also been attributed to direct occupational contact with infected animals. There is no evidence that any of the recorded clinical cases of human *M. bovis* infection in the UK which have occurred since 1994 were associated with recent consumption of contaminated dairy products or meat derived from *M. bovis* infected animals in the UK [12,13,14].

26. There have been no reported human outbreaks of *M. bovis* infection associated with unpasteurised milk or unpasteurised milk products in the UK for at least the last four decades.

Assumptions*

- No differences in infectivity between food products with the same number of *M. bovis* bacteria.
- No strain variation in infectivity.
- No significant variation in infectious dose of *M. bovis* from different species (i.e. cows, goats, sheep, buffalo)

Uncertainties*

- The proportion of *M. bovis* cases in the UK due to reactivation vs primary TB, (although the epidemiological evidence suggests that reactivated disease is responsible for most cases)[12,14].
- The infectious dose particularly for vulnerable groups/immunocompromised.
- The infectious dose of *M. bovis* in different food matrices – milk, cheese, etc.
- The effect of the 2005 change in BCG vaccination strategy. However a recent UK Zoonoses, Animal Diseases and Infections (UKZADI) paper using the incidence of tuberculosis in humans as a proxy measure of an increased risk in *M. bovis* infection in humans after discontinuation of the vaccination programme suggested no measurable effect, in terms of additional human cases of *M. bovis,* to date of the policy change.

Summary

27. In summary the infectious dose of *M. bovis* is thought to be high, in the region of millions of organisms by the gastrointestinal route. In most infections the disease is initially latent although at least 10% of those infected subsequently develop active tuberculosis with severe sequelae.

28. Clinical cases of human *M. bovis* in the UK are rare (e.g. 25 reported in 2009) and annual reported numbers have remained relatively low in England over the last few years[11]. No human outbreaks of *M. bovis* infection associated with unpasteurised milk or unpasteurised milk products have been reported in the UK for at least the last four decades.

*These are the main assumptions and uncertainties relevant to this assessment of risk as identified by the authors of this document. There may be additional assumptions and uncertainties involved.

4.0 Exposure Assessment *(the qualitative and/or quantitative evaluation of the likely intake of the hazard via food)*

Cows' milk and milk products

29. The potential exists for *M. bovis* to be present in unpasteurised milk or milk products if there is *M. bovis* infection in a dairy herd. If the herd happens to be producing raw milk for direct human consumption or for the manufacture of unpasteurised milk products a public health risk may arise until infection is detected in the herd by TB testing or slaughterhouse surveillance. The main risk arises from direct contamination of the milk in the udder, which is most likely when infection becomes disseminated in the animal leading to tuberculous mastitis.

30. The current bovine TB control programme in the UK minimises this exposure route through regular testing of herds, early detection and removal of infected cattle and exclusion of reactor milk (milk from cattle testing positive by the tuberculin skin test) from the food chain. Details of the TB controls in place in the UK for cattle are given in Annex 1. If TB is detected in a herd, either by a positive tuberculin skin test or through routine post-mortem meat inspection, the herd will automatically lose its Officially TB Free (OTF) status. This means that all TB test reactors and any at-risk direct contacts are required to be isolated and are compulsorily removed and slaughtered by the Animal Health and Veterinary Laboratories Agency (AHVLA) in GB. Milk from cows awaiting slaughter following a positive reaction to the tuberculin skin test (and in GB the interferon gamma blood test) is not permitted to go for human consumption. Milk from other animals in the herd must undergo pasteurisation (minimum 72°C for 15s) until herd OTF status is restored.

31. The number of cattle slaughtered annually under the TB control programme in GB has shown a marked increase from 10,000 animals slaughtered in 2000 to 36,000 in 2009. This rise has mainly been in England and Wales, with numbers in Scotland being low and stable, such that the European Commission granted Scotland officially tuberculosis free status in 2009. Numbers in N. Ireland for the same time period have peaked then declined, with 9,498 slaughtered in 2000 and 8,198 in 2009. Key data for *M. bovis* infection in cattle is given in Annex 2.

32. The potential for *M. bovis* to be present in milk cannot be totally eliminated due to i) the possible presence of anergic (infected but skin test negative) cattle and ii) the possible presence of cattle which have become infected between tuberculin skin tests. In both cases there is the potential for the animal to develop tuberculous mastitis and for contaminated milk to continue to enter the food supply whilst the herd maintains its OTF status. The attached influence diagram (ACM/1047b) outlines the factors that

influence the possible incidence and concentration of *M. bovis* in unpasteurised milk and milk products. These factors will be addressed below in turn.

Number of herds producing raw milk for human consumption (E1)

33. It is estimated there are 100 registered herds producing raw cows' drinking milk in the UK and around 100 more supplying milk for unpasteurised milk products[15] .The number of producing herds is therefore considered relatively small and has been declining in recent years (in England and Wales the number of herds producing raw cows' drinking milk has fallen from around 570 in 1997 to under 100 in 2011) Raw cows' drinking milk therefore represents only a small fraction of total UK milk production. There are no known sales in N. Ireland and sales in Scotland are banned. It is estimated that the average herd size for herds producing unpasteurised cows' drinking milk is 100[15a].

Number of infected animals in OTF herds producing raw milk for human consumption (E2, E2a,E2b, E2c)

34. As noted above, the presence of anergic individuals within herds means that it is possible for contaminated milk to continue to enter the food supply while the herd remains OTF. There may be a number of reasons why an animal is 'anergic', i.e. displaying a negative skin test but showing evidence of TB at slaughter (see Annex 3). The significance of anergic animals in respect of the production of contaminated milk is tempered by other control measures. For example, herds are subject to serial testing, all other cohort animals are tested simultaneously and the relationship between infection per se and contamination of the milk is considered minimal due to frequency of testing and the pathology of the disease. The sensitivity of the tuberculin skin test used in cattle in the UK has been reported to be between 52% and 100% (with a median value of 80%)[15b] and the bovine TB control programme will not and cannot be expected to immediately and accurately detect every infected animal, although this risk is mitigated in non-OTF infected herds by the fact that they will have to undergo several skin tests in short succession to regain their OTF status.

35. As noted above there is also the potential for animals to become infected (and subsequently infectious) during the period between routine herd tests. The likelihood of herds becoming infected between tests and the extent of subsequent spread within the herd is unknown and will depend on testing frequency, local prevalence of TB in cattle and wildlife reservoirs and herd husbandry/management practices. The frequency of testing varies by country, all herds in Wales are annually tested, in Northern Ireland, the interval is dependent on risk assessment, with a maximum interval of one year, in Scotland (which was declared an OTF region of the UK in October 2009) all herds are tested every four years and in England it has been a long

standing policy of AHVLA to place all dairy herds that are known to sell unpasteurised cows' milk directly to the consumer under an annual TB testing regime, regardless of the default routine frequency for other cattle herds in their locality. The frequency of testing combined with the chronic nature of the disease in cattle suggests it is unlikely that disease in an infected animal would occur and progress to tuberculous mastitis between herd tests.

Proportion of infected animals shedding *M. bovis* (E3, E3a)

36. Where there is infection in the herd, either detected or undetected, routes that could lead to contamination of raw milk with *M. bovis* include via faeces and from the environment but the main risk arises from direct contamination of the milk in the udder. Although shedding can occur before the animal tests positive on the skin test or interferon gamma test or before clinical signs of infection are apparent, this is rare. It is most likely to occur when infection becomes disseminated and there is tuberculous mastitis. In such cases large numbers of bacteria can be shed in the milk. However, evidence such as post-mortem findings, clinical reports and milk-borne spread to calves suggests that annual number of herds with cows' shedding *M. bovis* in their milk are quite rare in the UK nowadays, probably in the order of single figures. This is believed to be due to the fact that the current statutory bovine TB surveillance programme removes infected animals before the disease becomes disseminated to the udder.

37. The proportion of TB test reactors and slaughterhouse cases presenting with visible tuberculous lesions in the udder or the mammary lymph nodes in the course of post-mortem examination in 2010 was very small (0.05%), the proportion in the previous four years was similarly small (see Annex 4). The proportion in cows where disease has not yet been detected could be assumed to be even less. But using the figure of 0.05% it can be estimated that in 200 herds producing unpasteurised cows' milk with an average herd size of 100, only 10 cows (out of the 20,000) will have undetected tuberculous mastitis and potentially be shedding *M. bovis* into the milk. Assuming these cases are evenly distributed it can be estimated that, as a worst case scenario, 1 in every 20 herds producing unpasteurised cows' milk contains an animal shedding *M. bovis.*

Prevalence and concentration of organisms in raw bulk milk from an infected herd (E4)

38. It is not possible to accurately estimate the frequency (and trends) in shedding of *M. bovis* in infected cows' milk in the UK. However, only a small number of incidents of TB in dairy calves associated with exposure to contaminated milk from tuberculous cows are reported by AHVLA each year [16,17].

39. Use of a PCR method in a study to determine the number of bacilli present in milk from tuberculin positive cows estimated *M.*

bovis to be present at about 1000 organisms/ml[18]. Detection of *M. bovis* DNA by PCR does not necessarily reflect infectious bacteria and the concentration of organisms in milk from cattle where disseminated disease is not yet apparent is likely to be lower. However this figure can be used in worst case scenario models to estimate the concentrations of organisms being shed in the milk of undetected cases of tuberculous mastitis in cattle. A number of publications have suggested that atypically infected udders may excrete 500-500,000 *M. bovis* organisms/ml of milk [19].

40. There are no accurate UK level data on production volumes for raw drinking milk per herd. The average production yield per dairy cow per year reported in 2010/11 was 7406 litres/cow/year[19a] which can be averaged to 20 litres/cow/day. If the estimated number of cows in a herd is 100 the average herd might produce 2000 litres of unpasteurised milk/day.

41. As noted above (para 37) it can be estimated that 0.05% of cows in a herd may have undetected tuberculous mastitis and potentially be shedding *M. bovis* into the milk. For an average herd of 100 cows, with one animal with unrecognised tuberculous mastitis shedding 1000 organisms/ml, the concentration of *M. bovis* in bulk milk would be diluted approximately 100-fold i.e. to 10 *M. bovis* organisms/ml (or 10000 organisms/l). However it should be noted that with a tuberculous mastitis prevalence of 0.05% only 1 in every 20 herds producing unpasteurised milk will have a cow with tuberculous mastitis. The concentration of *M. bovis* in unpasteurised milk from the other 19 herds would be assumed to be 0.

<u>Prevalence and concentration of organisms in consumer units (E5, E5a, E5b)</u>

Milk

42. *M. bovis* is a slow-growing *Mycobacteria* with growth reported at 37°C but not at 25°C or 45°C in standard growth media[20]. It is generally considered not to multiply in milk so numbers are unlikely to increase significantly during the collection, storage and processing of any contaminated unpasteurised milk.

43. As a ‘worst case scenario’ there may be up to 10 bacilli/ml in bulk milk from an infected herd.

Milk products

44. Unpasteurised milk products are produced in the UK including cream, butter, yoghurt, ice cream, whey and cheese. Most are made from cows’ milk but some are made from buffalo, sheep or goats’ milk. The volumes produced from these species is difficult to estimate as production is very small scale with the exception of unpasteurised milk cheeses. Information from

membership of the Specialist Cheesemakers Association (www.specialistcheesemakers.co.uk) suggests there are currently as many as 57 manufacturers of raw milk cheeses in the UK the market for such products is growing.

45. As noted above (section 42) milk destined for production of milk products may be diluted with milk from other herds before use, and *M. bovis* numbers are not likely to significantly increase during collection, storage and initial processing. However less information is available in relation to the extent to which *M. bovis* can survive further processing into milk products such as such as cream, yoghurt, butter and ice cream. Some information is available on *M. bovis* survival in butter, cottage cheese[21] and fromage blanc (a product similar to thick yoghurt) where *M. bovis* is reported to survive for 14 days but not for 17 days (by which time this product is no longer suitable for consumption due to the development of mould contamination)[22]. This suggests that short shelf-life products could pose a risk to consumers as, if contaminated, they will be consumed while there are still viable bacteria present.

46. A wider body of work on survival in cheese has included studies on Emmental, Cheddar, Gruyere, Munster, Camembert[23] and Bleu d'Auvergne[24] (a blue cheese). Emmental has been particularly well studied and it has been shown that the production process has a considerable impact on longer term survival of *M. bovis*[23]. This may be due to the scalding process in which the curds are heated to 53°C for 30-40 minutes, which may reduce the ability on M. bovis to survive the period of cheese maturation.

47. Studies on other hard cheeses such as Cheddar show greater variability among the periods during which *M. bovis* may remain viable (approx. 60 days up to >200 days) [23]. As most cheddar cheeses are produced using a fairly standard process these differences in survival period may relate to different initial concentrations of *M. bovis* in the milk used. A number of early studies used milk containing unknown (and therefore potentially unrepresentatively high) initial concentrations of *M. bovis* leading to overestimation of the survival of *M. bovis* in stored cheeses. Nevertheless, there is evidence that *M. bovis* will not remain viable indefinitely in hard cheese.

48. To obtain better data on the survival of *M. bovis* in cheese, the FSA has been funding a research project on UK produced unpasteurised milk cheese, investigating survival of *M. bovis* through the manufacturing process and maturation. The research was designed to produce data on survival which would help inform risk assessments on unpasteurised milk cheese made with milk from herds which loose OTF status during the maturation process before the cheese is placed on the market.

49. The research undertaken focussed on two types of cheese – Caerphilly and Cheddar, as representative of semi-hard and hard cheeses with long maturation periods and therefore most likely to require a risk assessment if herd OTF status were to be lost.

The work involved manufacturing the cheese with milk inoculated with *M. bovis* and assessing survival through up to a year of maturation. Caerphilly can be matured for 2 weeks to 4 months and Cheddar for over a year in some cases. Based on the results obtained with high inoculum levels of *M. bovis* (10^6 cfu/ml), D_{10}* values were 58 days for Caerphilly and 48 days for Cheddar, indicating significant loss of *M. bovis* viability during the maturation period[25]. Low inoculum levels (10^3 cfu/ml *M. bovis*) D_{10} values were 15 days for Caerphilly and 35 days for Cheddar[26].

50. Assuming the level of *M. bovis* contamination in unpasteurised bulk milk used in the production of unpasteurised milk products is 10 *M. bovis* organisms/ml it is likely there will be at least a $\log_{10}$ reduction in bacterial numbers in cheeses such as Cheddar and Caerphilly after loss in the whey and maturation to around 1 organism/ml.

*D_{10} value is the time taken for a $\log_{10}$ reduction in bacterial numbers

Number of organisms ingested per consumption event (E6, E6a)

51. Data from the 2008/09 to 2009/10 National Diet and Nutrition Survey[27] (NDNS) reports the average (all consumers excluding 1.5 to 3 year olds) daily volume of semi-skimmed milk (the most popular type of milk) consumed in the UK is 152g or 152ml**. Assuming the average consumption of unpasteurised cows' milk per day is the same as the average consumption of semi-skimmed milk it is possible to estimate that a consumer may ingest a maximum of 1520 *M. bovis* organisms per consumption event (10 organisms/ml in 152ml) if the milk they consume has come from a herd with an animal with tuberculous mastitis. The average volume consumed per day has been taken as one consumption event as there is no data allowing this to be broken down further into individual serving sizes. As it is estimated that only in 1 in 20 herds contains an animal with tuberculous mastitis this is a worst case scenario and this level of exposure is estimated to occur on average every 1 in 20 exposure events.

52. For cheese the NDNS survey reports the average (all consumers excluding 1.5 to 3 year olds) daily volume of cheese consumed in the UK is 12.5g . Assuming the average consumption of unpasteurised cows' cheese is the same as the average consumption of all cheeses it is possible to estimate that a consumer may ingest a maximum of 12.5 *M. bovis* organisms per consumption event (1 organism/ml in 12.5ml) if the cheese they consume has come from milk from a herd with an animal with tuberculous mastitis. As this only occurs in 1 in 20 herds this is a worst case scenario and this level of exposure will only occur on average every 1 in 20 exposure events. This calculation has only been performed for cheese as this is likely to be the most significant unpasteurised cows' milk product consumed.

53. It is not possible to calculate the number of organisms ingested per consumption event on a UK population basis as the number of consumers of unpasteurised cows' milk and milk products are unknown. The sale of raw cows' drinking milk is subject to certain restrictions and labelling requirements in England, Wales and N. Ireland and it is thought that relatively few people buy and consume raw cows' milk in England and Wales (there are no know sales in N. Ireland).

**The density of milk varies for different types but is around 1.03kg/m^3 for semi-skimmed milk. For the purposes of this rough calculation a density of 1.0 is assumed so weight can be converted directly to volume.

Assumptions:

- Only animals with tuberculous mastitis shed *M. bovis* into their milk
- Milk production volumes are the same in healthy animals and those shedding *M. bovis* although severe mastitis is likely to involve a reduction in milk production.
- The volume of unpasteurised milk consumed per person is the same as the average volume of semi-skimmed milk consumed/person/day
- The volume of unpasteurised milk cheese consumed per person is the same as the volume of all cheeses consumed/person/day.
- The average herd size is 100 cows/herd in herds produced unpasteurised milk.
- The frequency of shedding for all cows with tuberculous mastitis is similar.
- The level of contamination in unpasteurised milk for drinking and for the production of milk products is the same.

Uncertainties:

- The number of anergic cows in a herd.
- The number of bacilli shed by anergic animals.
- The likelihood of herds becoming infected between tests and subsequent spread within the herd.
- The number of consumers who drink unpasteurised milk or eat unpasteurised milk products and the volumes they consume.

Buffalo milk and milk products

54. The TB controls on buffalo herds are essentially the same as the controls for dairy cows – see Annex 1. Animals are subject to a tuberculin skin testing programme and milk from herds which have lost their OTF status is required to go for pasteurisation. As with dairy cows the main risk of contamination arises from disseminated *M. bovis* infection in the animal and tuberculous mastitis. The control programme aims to reduce this risk through early detection and removal of infected buffaloes. The potential for anergic animals to exist in the herd remains as does the potential for animals to become infected and shed *M. bovis* into raw milk between tuberculin tests. The frequency of tuberculous mastitis in buffaloes and the prevalence of anergic buffaloes is not known and therefore it is difficult to estimate the number of infected animals that may be present in an OTF herd and the proportion that may be shedding *M. bovis*.

55. No current data on the number of producing herds was found although there are likely to be far fewer than the number of dairy herds producing unpasteurised cows' milk, possibly in the region of 5-20 herds in the UK and herd size could range from 100 to 400 animals[28]. Production volumes per herd or for the UK are not known but buffalo are reported to produce less milk per animal than cows. The prevalence and concentration of *M. bovis* in raw bulk milk from an infected buffalo herd is therefore difficult to estimate and no studies measuring the concentration of *M. bovis* in buffalo milk were identified. Any contaminated milk would be diluted with milk from healthy animals in the herd.

56. There are no restrictions on the sales of unpasteurised buffalo milk in England and Wales. In Wales there is a requirement for the milk to carry the health warning. In Scotland sales are banned and there are no known sales in N. Ireland.

57. *M. bovis* is considered not to multiply in milk so numbers are unlikely to increase during the storage of any contaminated buffalo milk. Studies on the survival of *M. bovis* in buffalo milk products were not found. As production volumes are much smaller for unpasteurised buffalo milk and milk products compared to that for unpasteurised cows' milk and milk products the number of potential exposure events will be much fewer.

Sheep and goats' milk and milk products

58. Sporadic incidents of TB caused by *M. bovis* arise in non-bovine dairy species (sheep and goats) and occur almost invariably in areas of endemic high incidence of TB in cattle and wildlife. In GB, TB in farmed animals other than cattle is also notifiable and when a culture-confirmed episode of *M. bovis* infection is disclosed in those species, movement restrictions are immediately applied on the herd/flock of origin and a veterinary risk assessment of the premises is carried out by AHVLA to inform the need for further action. As with all confirmed incidents of *M. bovis* infection in cattle, AHVLA will also inform the Consultant in Communicable Disease Control of the Local Health Protection Unit. If dairy goats or sheep are involved, the Local Food Authority is also notified. Movement restrictions remain in place until the entire affected herd or epidemiological group has been slaughtered or after repeat tuberculin skin testing as required by AHVLA has been completed with removal of any test reactor animals. In England, *ante mortem* TB testing of these species is voluntary and there is no compensation to herd owners for the slaughter of test reactors. Similarly in Wales there is no routine *ante mortem* testing of sheep and goats although powers to require TB testing are in place as well as statutory compensation for any goats removed as test reactors.

59. In NI, bovine TB in other species is notifiable. No action is taken in respect of movement restriction, disease control or testing and compensation in these species outside the risk they pose to bovines. If they are considered significant in a bovine episode, restrictions on movements and disease control measures are placed on the cattle herd as required.

60. In England and Wales there are no restrictions on sales of unpasteurised sheep or goats' milk to the consumer but the milk is required to carry the same health warning as unpasteurised cows' milk. Production is small scale with 27 producers registered with AHVLA known to sell raw goats drinking milk and 3 known to sell sheep milk. Sales of raw drinking milk and cream from any species are banned in Scotland. Northern Ireland has similar controls to England and Wales but there are no known sales.

61. The legislative requirements in Regulation (EC) 853/2004 for species other than cows and buffaloes which are susceptible to TB requires that raw milk from sheep and goats must come from herds which are regularly checked for this disease under a control plan that the competent authority has approved. A control plan to enact this legislative provision is under development by the FSA in discussion with the agriculture departments of the UK. In the meantime, AHVLA will only test goats for TB whenever *M. bovis* infection is found in a co-located cattle herd or *M. bovis* infection is confirmed in a goat herd. DARD has no control programme directed at disease control in other species.

62. When considering the potential for *M. bovis* to be present in sheep and goats milk there is significantly less information available on the level of infection in these animals because they are not currently routinely tested under a control programme. However,

as there are only sporadic reported incidents of TB in such flocks/herds, this suggests that the incidence is low and therefore the likelihood of animals with disseminated disease supplying contaminated milk into the foodchain is also low. No studies measuring the concentration of *M. bovis* in milk from infected sheep or goats were identified therefore the concentration of *M. bovis* in raw bulk milk from an infected sheep or goat herd is difficult to estimate but any contaminated milk would be diluted with milk from healthy animals in the herd. *M. bovis* is considered not to multiply in milk so numbers are unlikely to increase during the storage of any contaminated sheep or goats' milk. Studies on the survival of *M. bovis* in sheep or goats' milk products were not found. As production volumes are much smaller for unpasteurised sheep or goats' milk and milk products compared to that for unpasteurised cows' milk and milk products the number of potential exposure events will be much fewer.

Uncertainties

- TB prevalence in buffalo, sheep and goats in the UK
- The frequency of tuberculous mastitis in buffaloes, sheep and goats and the prevalence of anergic animals
- The number of *M. bovis* organisms shed by infected sheep, goats and buffaloes
- Herd size and volumes produced for unpasteurised buffalo, goat and sheep milk and milk products
- Prevalence and concentration of *M. bovis* in unpasteurised buffalo, goat and sheep milk and milk products
- Survival of *M. bovis* in unpasteurised buffalo, sheep and goat milk products.
- The number of consumers who drink unpasteurised milk or eat unpasteurised milk products from buffalo, sheep and goats and the volumes they consume.

Summary

63. The potential for *M. bovis* to be present in unpasteurised cows' milk destined for human consumption is minimised through regular TB herd testing, early detection and removal of infected cattle and exclusion of reactor milk from the food chain. The risk cannot be totally eliminated due to the possibility of infection of cattle between herd tests and the presence of anergic cattle. As these anergic cattle are not detected by the skin test they remain in the herd during which time they may develop tuberculous mastitis and continue to supply contaminated milk into the food chain. However, the significance of anergic cattle in the contamination of milk is believed to be low. Other indicators of infection in the herd such as cohort disclosure would result in the loss of OTF status and the milk would not be permitted to be sold unpasteurised for direct human consumption. Despite the resurgence of bovine TB in cattle since the late 1980's, tuberculous mastitis is rarely seen in the UK as the surveillance programme means that infected animals tend to be removed from the herd in the relatively early stages of infection as herds

undergo repeat annual tests. Data on the concentration of *M. bovis* in milk from infected animals combined with an estimate of the number of infected animals shedding *M. bovis* in a herd allowed a calculation of 1520 organisms ingested per consumption event for every 1 in 20 exposures to unpasteurised cows' milk. This is likely to be an overestimate as it is calculated on a worst case scenarios basis. It was not possible to calculate exposure on a population basis as the number of consumers of unpasteurised cows' milk is unknown but there are thought to be relatively few consumers due to sales restrictions.

64. There is little evidence on survival of *M. bovis* in unpasteurised products other than cheese. The available evidence shows *M. bovis* can survive the production process and persist in short shelf life products. It also supports the possibility that if cheese is manufactured from unpasteurised milk contaminated with high concentrations of *M. bovis* this organism can survive the production process and persist through some stages of the maturation process. *M. bovis* viability declines during maturation at rates influenced by the physical parameters of the cheese (pH, water activity, salt) and the length of maturation and therefore the exposure to *M. bovis* in cheese is likely to be less than for milk. An estimate of the concentration of *M. bovis* in unpasteurised cows' milk used in the production of unpasteurised milk products allowed a calculation of 12.5 *M. bovis* organisms ingested per consumption event for every 1 in 20 exposures to unpasteurised cows' milk cheese.

65. The potential exists for *M. bovis* to be present in unpasteurised milk or milk products from sheep, goats and buffalo if there is *M. bovis* infection in a herd producing raw milk for direct human consumption or for the manufacture of unpasteurised milk products. The main risk arises from direct contamination of the milk in the udder, which is most likely when infection becomes disseminated in the animal leading to tuberculous mastitis. For buffalo there is little data on which to base an estimate of the number of *M. bovis* organisms ingested per consumption event. There is nothing to suggest this would be higher than for unpasteurised cows' milk or milk products and given the lower production volumes exposure is likely to be less. Similarly there is little data on which to base an estimate of the number of organisms consumed in unpasteurised sheep and goats' milk and milk products. TB outbreaks in sheep and goats are sporadic so it is assumed the prevalence of TB mastitis is much lower than in cattle. Combined with the lower production volumes for milk and milk products from goats and sheep the exposure to *M. bovis* is likely to be less than for cows' milk and milk products.

5.0 Risk Characterisation *(The process of determining the qualitative and/or quantitative estimation, including uncertainties, of the probability of occurrence and severity of known or potential adverse health effects in a given population based on information from the hazard identification, exposure assessment and hazard characterisation. See Annex 5 for the assessed levels of risk considered in this risk assessment).*

66. There is a risk to human health from consumption of *M. bovis* contaminated unpasteurised milk if there is *M. bovis* infection in a herd producing raw milk for direct human consumption. For unpasteurised cows' milk the level of risk is considered very low as the likelihood of consumers being exposed to sufficient organisms in raw milk to cause infection is very rare but cannot be excluded. The maximum number of organisms to which an individual could be exposed in 20 consumption events was estimated to be around 1500 organisms where the infectious dose for human is estimated to be in the region of millions of organisms by the gastrointestinal route. Additionally the BCG vaccine is regarded as providing some level of protection against *M. bovis* and most UK adults will have been vaccinated as children. Should human infection be established the likelihood of active TB developing is approximately a 10% lifetime risk. The infectious dose for vulnerable groups is unknown but it is generally advised that these groups should not consume unpasteurised milk and in Wales this warning is specifically included on the labelling of unpasteurised milk.

67. Exposure of consumers to *M. bovis* in unpasteurised milk from sheep, goats and buffaloes is likely to be less than for unpasteurised cows' milk due to the smaller production volumes and probable lower prevalence of TB in these species. However there are more uncertainties associated with this assessment due to a lack of data on which to base a quantitative assessment and therefore the level of risk is considered very low rather than negligible.

68. There is a risk to human health from consumption of *M. bovis* contaminated milk products if there is *M. bovis* infection in a herd producing raw milk for the manufacture of unpasteurised milk products. For unpasteurised cows' milk products the level of risk is considered very low as the likelihood of consumers being exposed to sufficient organisms in raw cows' milk products to cause infection is very rare but cannot be excluded. The maximum number of organisms to which an individual could be exposed from unpasteurised cows' milk cheese in 20 consumption events was estimated to be less than 13 organisms where the infectious dose for human is estimated to be in the region of millions of organisms by the gastrointestinal route. Other unpasteurised milk products were not assessed but cheese was considered to be the most significant route by which consumers may be exposed to *M. bovis*. Additionally the BCG vaccine is regarded as providing some level of protection against *M. bovis* and most UK adults will have been vaccinated as children. Should human infection be established the likelihood of active TB developing is

approximately a 10% lifetime risk. The infectious dose for vulnerable groups is unknown but it is generally advised that these groups should not consume unpasteurised milk products.

69. Exposure of consumers to *M. bovis* in unpasteurised milk products from sheep, goats and buffaloes is likely to be less than for unpasteurised cows' milk products due to the smaller production volumes and probable lower prevalence of TB in these species. However there are more uncertainties associated with this assessment due to a lack of data on which to base a quantitative assessment and therefore the level of risk is considered very low rather than negligible.

70. The fact that there are few clinical cases of human *M. bovis* reported annually in the UK (25 reported in 2009) and this number has remained relatively stable in England over the last few years with no evidence that any of the recorded UK cases of human *M. bovis* infection which have occurred since 1994 have been acquired through recent consumption of contaminated meat or dairy products derived from *M. bovis* infected animals in the UK provides some confidence in our estimation of the risks from unpasteurised milk and milk products.

Conclusions

- **The risk of human TB infection acquired from unpasteurised milk and milk products has changed with the increase in *M. bovis* in cattle.**

- **The risk to human health from *M. bovis* in unpasteurised cows' milk and milk products is very low.**

- **The risk to human health from *M. bovis* in unpasteurised sheep, goat and buffalo milk and milk products is likely to be very low but due to a lack of data on these species there are more uncertainties associated with this assessment.**

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Annex 1

The sections below outline the main components of the bovine TB control programme in the UK and controls on sales to the consumer.

TB controls in cows and buffaloes

1. The current bovine TB control programme in the UK, which applies to cows and buffaloes, is designed to detect *M. bovis* infection in the national herd by routine testing of herds at variable intervals, additional targeted testing of herds and animals at risk and by post mortem inspection of all animals at slaughter by FSA meat inspectors and official veterinarians.

2. The cornerstone of the TB control programme is the routine tuberculin skin testing of cow and buffalo herds performed according to a frequency (annual to 4-yearly) dictated by the local incidence of TB herd breakdowns. All herds in Wales are annually tested. In Northern Ireland, the interval is dependent on risk assessment, with a maximum interval of one year and over 25% of herds tested more frequently. In Scotland, which was declared an Officially TB Free (OTF) region of the UK in October 2009 by the European Commission, all herds are tested every four years. In England, the area and number of herds under annual testing has markedly increased since the beginning of 2010 relative to previous years. As a result of this change, 47% of all English herds are now annually tested and 11% are tested every two years. Additionally it has been a long standing policy of AHVLA in England and Wales to place all dairy herds that are known to sell unpasteurised cows' milk directly to the consumer under an annual TB testing regime, regardless of the default routine frequency for other cattle herds in their locality.

3. If TB is detected in a herd, either by use of the skin test or through routine post-mortem meat inspection, the herd will automatically lose its OTF status. All tuberculin skin test reactors and any at-risk direct contacts are required to be isolated and are compulsorily removed and slaughtered by the Animal Health and Veterinary Laboratories Agency (AHVLA) in GB. Herds with test reactors and/or slaughterhouse cases undergo movement restrictions, epidemiological investigations and whole herd testing at 60 to 90-day intervals in order to regain their OTF designation. The more sensitive gamma interferon blood test is deployed as an ancillary parallel test in some herds with culture-confirmed *M. bovis* infection that fulfil certain criteria. Depopulation of whole herds or groups of severely infected animals takes place very occasionally.

Controls on unpasteurised milk sales to the consumer

4. Sale of unpasteurised cows' milk direct to the consumer is permitted in England and Wales, however fewer than 100 retailers now exist compared to several hundred in 2001. The sale of unpasteurised cows' milk to consumers is confined to farm gate sales, farm catering, milk rounds and farmers markets. It is also known that two producers offer internet sales. All such milk must carry the health warning 'This milk has not been heat treated and may therefore contain organisms harmful to health'. In Wales, the warning also highlights the risks to vulnerable groups.

5. In England and Wales there are no restrictions on sales of unpasteurised buffaloes' milk to the consumer and in Wales is there a requirement for the milk to carry the health warning.

6. Sales of raw drinking milk and cream from cows and buffaloes are banned in Scotland. Northern Ireland has similar controls to England and Wales but there are no known sales.

7. For cattle herds in England and Wales whose milk is sold unpasteurised direct to the consumer, public health protection is provided through Regulation (EC) 853/2004, which requires that raw cows' and buffaloes' milk for human consumption shall only come from animals belonging to an OTF herd, i.e. where there is no evidence of *M. bovis* infection. Additionally, although not part of the food hygiene regulations, it has been a long standing policy of AHVLA in England and Wales to place all dairy herds that are known to sell unpasteurised cows' milk directly to the consumer under an annual TB testing regime, regardless of the default routine frequency for other cattle herds in their locality.

8. If the OTF status of a dairy herd is suspended or withdrawn (e.g. when test reactors or slaughterhouse cases are detected or when a TB test becomes overdue), AHVLA will immediately notify the relevant Local Food Authority, who are responsible for enforcing compliance with the food hygiene regulations. At the time of suspension of OTF status, the affected herd owner (food business operator) is also informed by AHVLA in writing of their legal obligations in respect of the marketing of milk from their herds. Milk from animals giving a positive reaction to the tuberculin test is not permitted to go for human consumption. Milk from other animals in the herd must undergo pasteurisation (minimum 72°C for 15s) until the OTF status is restored. The control programme in Northern Ireland works on broadly similar principles.

Controls on unpasteurised milk products

9. For cattle herds in England and Wales whose milk is used to produce unpasteurised milk products, public health protection is provided through Regulation (EC) 853/2004, which requires that raw cows' and buffaloes' milk for human consumption shall only come from animals belonging to an OTF herd, i.e. where there is no evidence of *M. bovis* infection. The frequency at which such herds are tested will be dictated by the local incidence of TB but AHVLA place individual herds on an annual testing regime, where they have knowledge that the milk is used to produce unpasteurised milk products.

10. In cases where herds providing milk to raw milk cheesemakers lose their TB free status, the local food authority will carry out a risk assessment on the public health implications for any products made prior to the loss of status and any control measures necessary. This assessment is undertaken locally with the Consultant in Communicable Disease Control (CCDC) and Animal Health. Guidance issued to Local Authorities by the FSA sets out detailed information on the factors to take into account when making such a risk assessment e.g. the TB history of the herd, the number of reactors found, whether the reactors were milk producing animals and tissue culture results[1].

11. Advice on the investigation and management of potential human contacts is included in guidance issued to CCDCs and Chief EHOs by the National Institute of Clinical Excellence. Screening is generally recommended only in the case of those less than 16 years old who have not been vaccinated and who may have consumed unpasteurised milk or dairy products from affected animals with proven or possible udder infection.

[1] Food Law Practice Guidance (England) ANNEX 8, APPENDIX 1: Guidance to Food Authorities in England on Officially Tuberculosis Free Status and Dairy Hygiene Legislation (Similar guidance exists in the equivalent documents for Scotland Wales and N. Ireland)

Annex 2

M. BOVIS INFECTION IN CATTLE

1. Bovine TB (bTB) remains the most serious endemic disease affecting the cattle industry in the UK. The distribution of infected herds is geographically clustered in the South West and Midlands of England and South and Mid-Wales, whereas TB breakdowns or incidents[2] occur only sporadically in the North and East of England and Scotland, often associated with movements of infected cattle from the endemic bTB regions (see Figure 1).

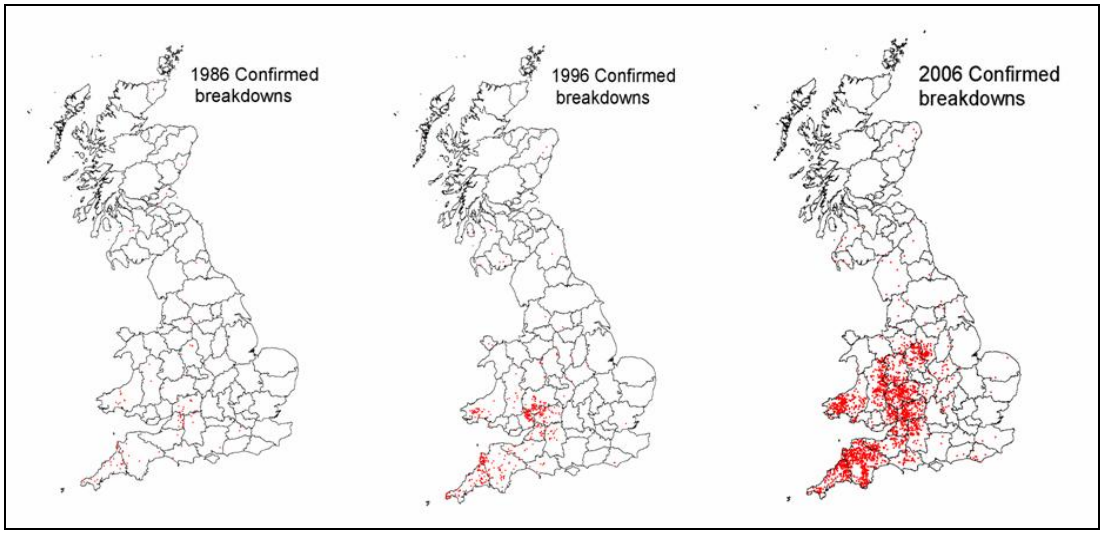

Figure 1 - Geographical distribution of all confirmed new bTB incidents identified in GB in 1986, 1996 and 2006 (source: VLA).

2. In Northern Ireland (NI) the herd incidence of bTB peaked in 2001/2002 at about 10%, has declined to about 5.5% and remained at this level for the past two years (see Fig 2). Whilst there are areas with higher herd incidence, the disease is less geographically demarcated than in GB.

3. Key bTB statistics for GB are presented in Figures 3 to 5 below. Due to the impact of the suspension of tuberculin testing during most of 2001 (due to a major outbreak of Foot and Mouth Disease), data for that year are not comparable with other years. Similarly, due to testing cattle backlogged from 2001, the 2002 data are also not comparable. Since the 2001 FMD outbreak there has been a significant increase in the number of reactors and breakdowns, which is thought to have been caused by the cessation of routine testing and higher prevalence in cattle and badgers. The incidence of new TB breakdowns confirmed by culture increased in GB from 3.5% in 2003 to 5.0% in 2008. Data for 2009 show that the number (and incidence) of herd breakdowns have declined compared to 2008 but increased again in 2010. It is too early to tell whether this trend will be sustained in coming years.

[2] A breakdown or incident occurs when one or more reactors are found in a herd.

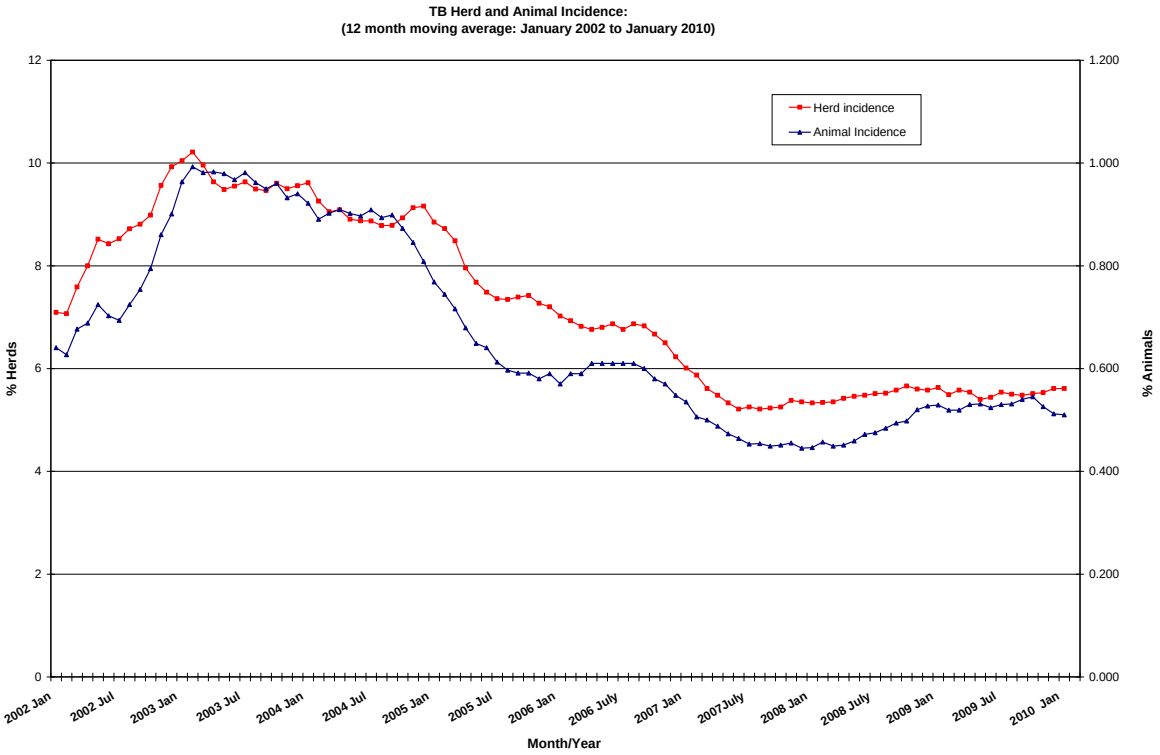

Figure 2 - TB herd and animal incidence in N. Ireland (12 month rolling average) Jan 02- Jan 10

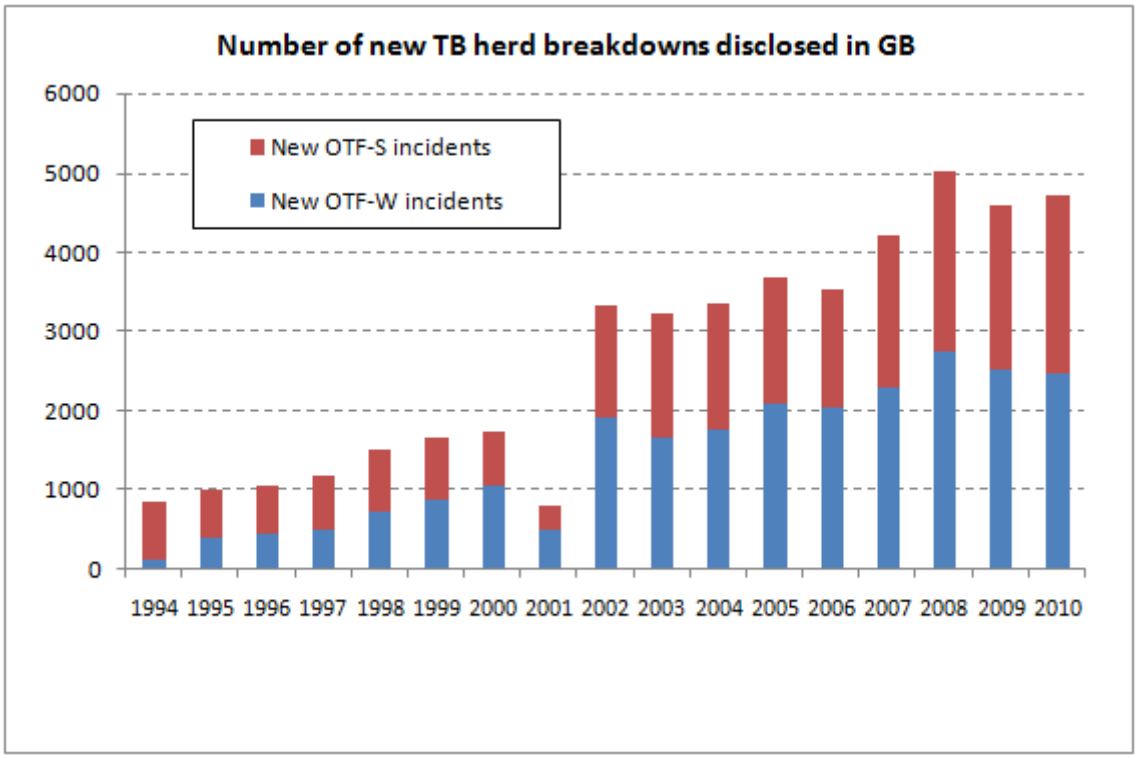

Figure 3 - Number of new bTB incidents (herd breakdowns) disclosed annually in GB (1994-2010) (source: Defra).

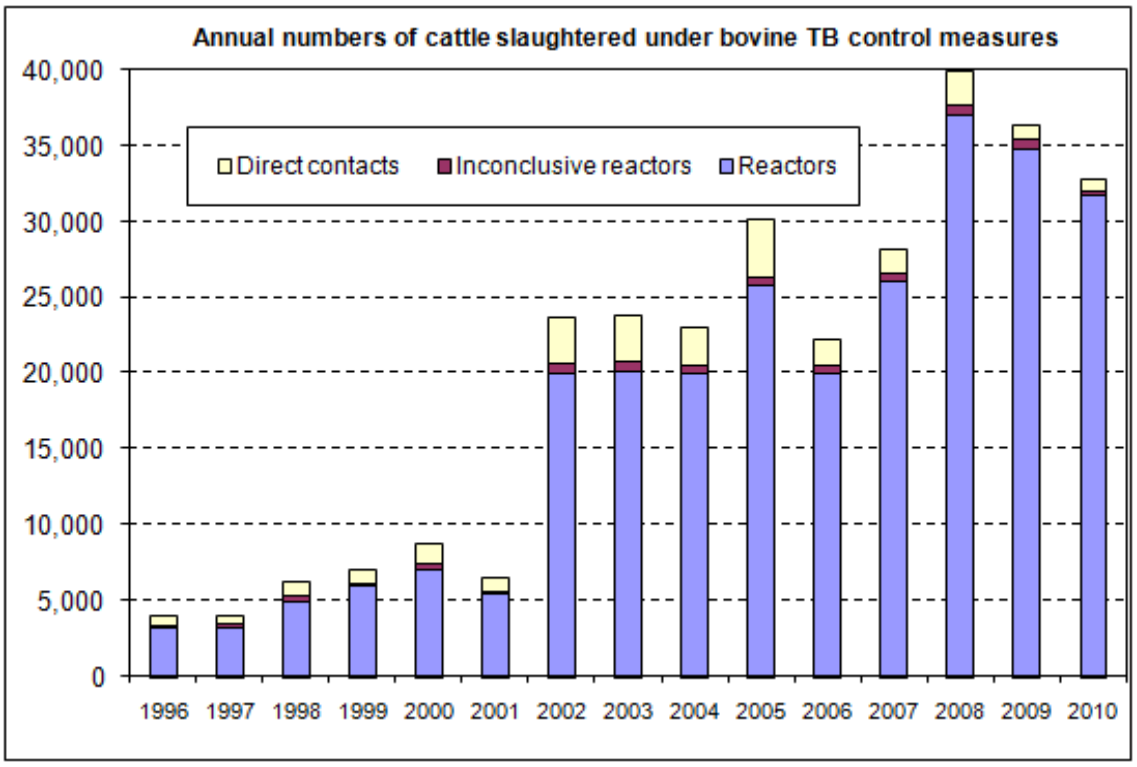

Figure 4 – Number of cattle slaughtered annually under the bTB control programme in GB (1996 – 2010) (source: Defra)

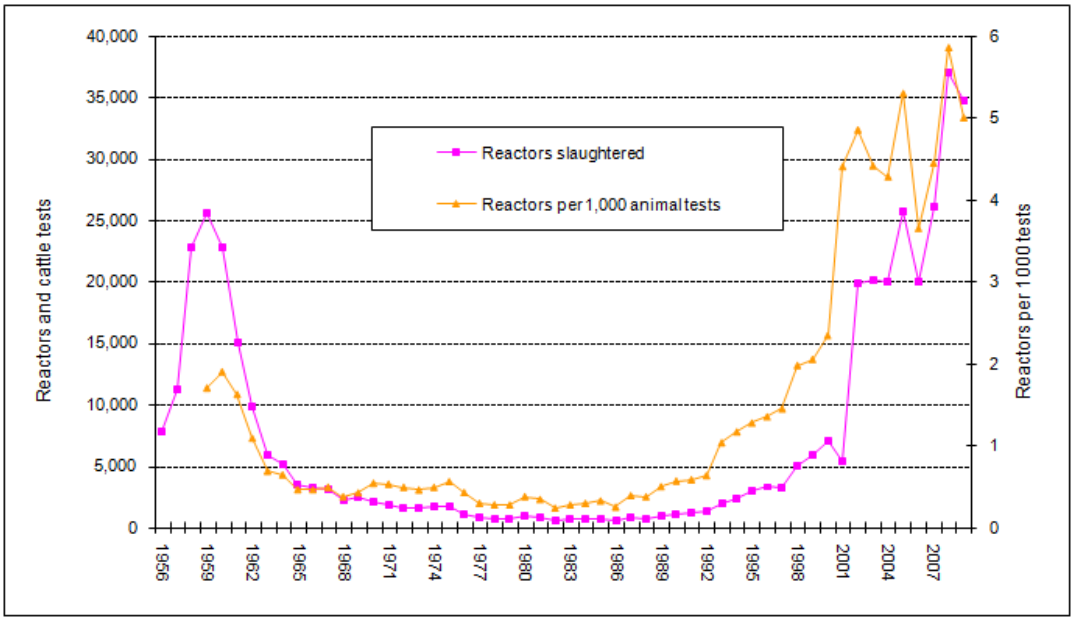

Figure 5 - Number (and rate per thousand cattle tests) of tuberculin test reactors disclosed annually in GB (1956-2009) (source: CVO annual reports, Defra).

Current position

Great Britain

4. The current bTB control programme in GB is designed to detect *M. bovis* infection in the national cattle herd by routine testing of herds, slaughterhouse inspection of cattle carcases and targeted testing of herds and animals at risk. The cornerstone of the programme continues to be the routine tuberculin skin testing of cattle herds managed by Animal Health and performed according to a frequency (annual to 4-yearly) dictated by the local incidence of bTB herd breakdowns. All test reactors and contacts are compulsorily removed. Herds with test reactors and/or slaughterhouse cases undergo movement restrictions, short-interval testing and epidemiological investigations, and occasional depopulation of severely infected units or groups of cattle.

5. The vast majority[3] of cattle slaughtered for bTB control purposes undergo post-mortem examination at approved abattoirs and carcases are judged as to their fitness for human consumption in accordance with EU food hygiene regulations (Regulation (EC) No 854/2004). A representative sample of reactors from each affected herd also undergo fresh tissue sampling for mycobacterial culture and molecular typing of *M. bovis* isolates at VLA as an aid to on-farm outbreak investigations.

6. The proportion of test reactors slaughtered in GB with demonstrable evidence of *M. bovis* infection at post-mortem examination continues to change over time. In the latter years it has fluctuated between 30% and 40%, compared with 50-60% during the 1990s and 2000 (Figure 6).

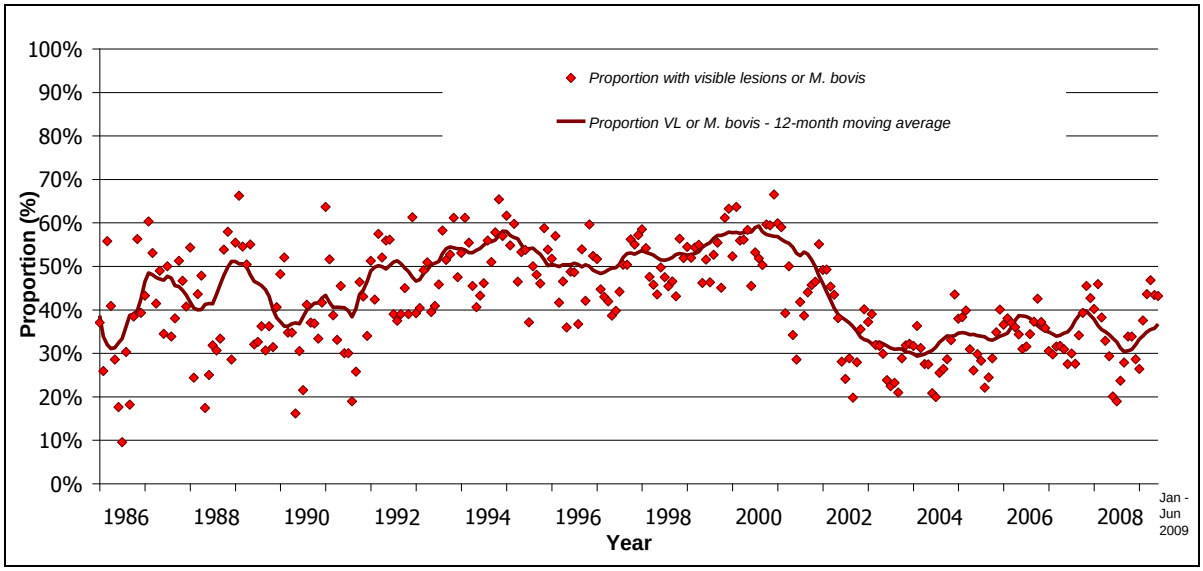

Figure 6 - Overall "confirmation rate" for reactor cattle removed by Animal Health in GB per month, between January 1986 and June 2009. The mean reactor confirmation rate in the period July 08 - June 09 was 34% (s.d. 9.0%) (source: VLA).

[3] A very small proportion will not be fit for human consumption due to having recently been given veterinary medicines and still being within the withdrawal period.

7. This active, on-farm bTB surveillance regime is supplemented by routine meat inspection of non-reactor cattle at commercial slaughter by the Food Standards Agency. Cases from this stream account for approximately 10% of total new bTB incidents.

8. In response to the increase in bTB over the last decade a number of specific enhancements to this programme have been introduced. These include a marked expansion of the areas under annual TB testing and, as a result, the total number of herds and animals tested (Figure 7), enhanced bTB surveillance arrangements in a 3 km radius around new confirmed breakdowns and more rigorous bTB testing schedules introduced for new and re-formed cattle herds. Additionally, compulsory pre-movement tuberculin skin testing of cattle was introduced in Scotland in September 2005, England (March 2006) and Wales (May 2006), which targets movements of cattle from herds in the higher incidence areas. The gamma interferon blood test was rolled out in October 2006 as an ancillary parallel test to improve the sensitivity of the TB testing regime in defined situations. From 2010 (March 2009 in Scotland and Wales) the number of re-tests allowed for inconclusive reactors has been reduced from two to one.

9. On 8 September 2009 the European Commission granted Scotland officially bovine tuberculosis free (OTF) status, reflecting the low and stable incidence of bTB in Scottish herds. Given the ongoing risk of bTB incursions from neighbouring countries, and as the majority of recently disclosed new confirmed incidents in Scotland have been found in cattle introduced from neighbouring countries, controls on movements of cattle into Scotland remain in place to protect this regional OTF status. These are mainly in the form of statutory pre- and post-movement tuberculin skin testing for live cattle imported from England, Wales, Northern Ireland and the Republic of Ireland.

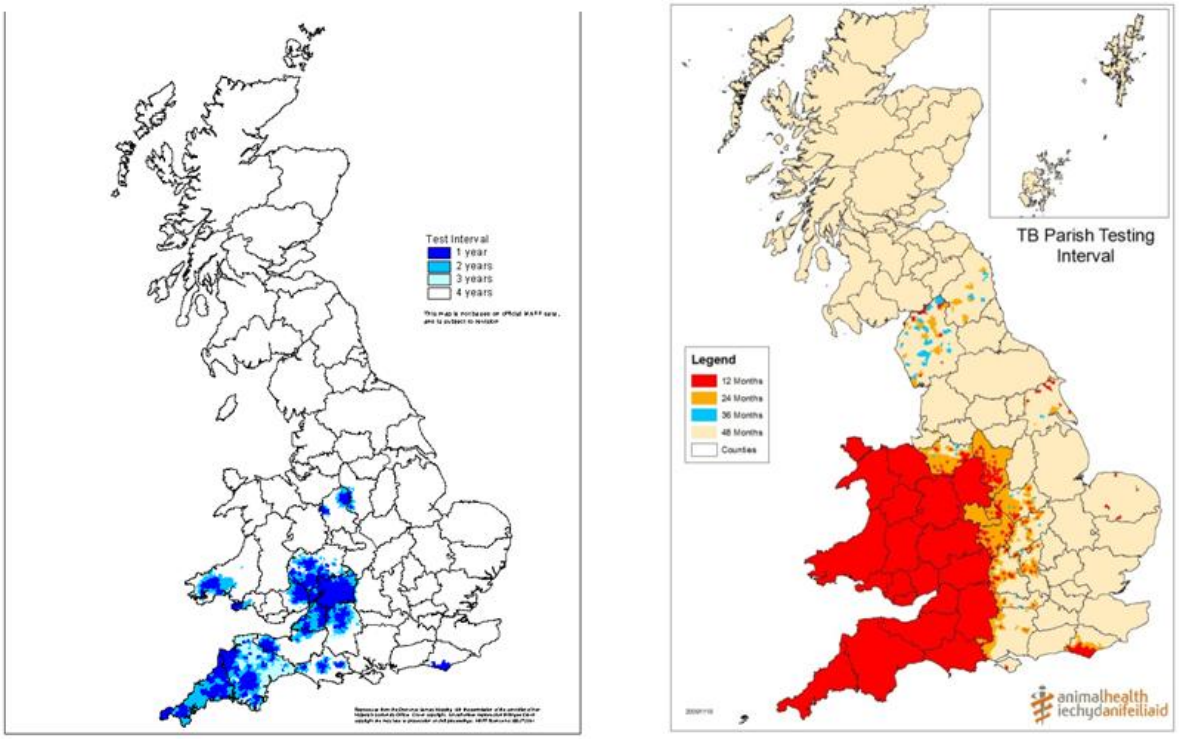

Figure 7 – Routine herd bTB testing frequencies in GB in 2000 (left) and 2010 (right). The maps illustrate the expansion of annual testing areas in the last 10 years, but please note the different colour schemes representing the four testing frequencies on both maps.

Northern Ireland

10. Live animal surveillance, controlled by the Department of Agriculture and Rural Development (DARD), is primarily based on the tuberculin skin test, supplemented where required by the ancillary gamma interferon blood test. Routine surveillance requires a herd test within 1 year. However, just under 30% of herds in NI undergo more frequent testing as a result of epidemiological investigations. From 2004, live animal movement control restrictions are automatically placed on herds that do not complete a herd test within this time. Failure to test cattle within 13 months attracts a further restriction on movement to slaughter.

11. All reactors disclosed by live surveillance are compulsorily removed by DARD and slaughtered in one contracted abattoir. Movement restrictions are applied to the herd and epidemiological investigation and tracing is undertaken. Depopulation may occur where considered necessary for disease control.

12. Between January 2007 and December 2009, 37,024 animals underwent gamma interferon blood testing, of which 2734 (7.4%) gave a positive result. This is out of a total cattle test population of about 1.6 million. Of these 2134 (5.8% of total tested) were not tuberculin skin test reactors and 1386 (64.9%) of these were voluntarily slaughtered.

13. During 2008, there were 1,067 animals detected with suspect TB lesions at routine slaughter with 640 (60%) confirmed through the culture of *M. bovis*. This

is out of a total cattle test population of about 1.6 million. Of the 1,412 herds with confirmed bTB infection during 2008, 340 herds (21.6%) had TB confirmed through animals with lesions at routine slaughter only.

Annex 3

Anergic Cattle

1. Under the widest definition of anergic, this may be the result of a poor skin testing technique, use of tuberculin of reduced potency, desensitisation after injection of tuberculin, immunosuppression during early post-partum, due to the administration of certain drugs or co-infections with certain parasites and viruses. A proportion of those anergic animals will be detected by the gamma-interferon blood test.

2. The narrower definition of anergy is when visibly infected cattle fail to react to the tuberculin test due to changes in the host's immunopathological response in the advanced disease stages of TB, when the bacteria "break out" of the primary lesions at their point of entry and disseminate throughout the body. In those cases, the cell-mediated immune response measured by the skin and gamma-interferon tests is gradually replaced by circulating antibodies against *M. bovis* and this requires a different type of immunological test (so-called serological or antibody assays).

3. The serum antibody assay currently available for bovine TB diagnosis in GB is the Chembio Stat-PAK rapid test. This assay has been validated in cattle, but it has a low sensitivity (other than for animals with advanced TB lesions) and is only used by AHVLA in very exceptional circumstances and with the herd owner's consent. Other antibody-based tests have been developed in the USA and Ireland and are undergoing validation by AHVLA. However, for the time being antibody tests are not officially approved by the EU, either for routine TB screening of cattle or as ancillary tests.

4. By definition, it is difficult to know when a herd contains anergic animals due to advanced TB and, by implication, when to deploy the serological tests but, in general, it is believed that those cases are quite rare and AHVLA will use serology only when there is evidence of ongoing cattle-to-cattle spread in a chronically infected herd despite the repeated application of the tuberculin and gamma-interferon tests (e.g. herds with a high incidence of TB in young calves associated to milk-borne spread from a tuberculous mastitic cow). The antibody assay may be used in NI where considered beneficial for disease control in a herd, but this is infrequent.

Annex 4

Total tissue samples from TB reactor cattle and slaughterhouse cases submitted to VLA for mycobacterial culture (2003-July 2010)

Sex	Lesions	**Total**	2003	2004	2005	2006	2007	2008	2009	2010
Undefined	Total	**10**	1	1	2	1	1	1	3	
	NVL	**2**			1	1				
	VL	**8**	1	1	1		1	1	3	
Male	Total	**19862**	525	2997	3491	2611	2649	3589	2600	1400
M	NVL	**10005**	166	1626	2001	1304	1306	1904	1161	537
M	VL	**9857**	359	1371	1490	1307	1343	1685	1439	863
Female	Total	**92287**	2930	15878	16040	11580	12965	15780	11647	5467
F	NVL	**62601**	1441	11572	11706	7726	8979	10879	7308	2990
F	VL, split as follows:	**29686**	1489	4306	4334	3854	3986	4901	4339	2477
	Lymph nodes	**27920**	1392	4026	4092	3657	3762	4626	4038	2327
	(of which *M.bovis* positive)	**26059**	1216	3724	3829	3464	3503	4330	3772	2221
	Organs	**1473**	67	231	197	170	192	223	260	133
	(of which *M.bovis* positive)	**1262**	55	189	162	153	168	190	225	120
	Other	**161**	6	33	17	22	19	37	17	10
	(of which *M.bovis* positive)	**87**	5	14	13	9	5	21	13	7
	Udder	**58**	1	4	22	2	4	7	13	5
	(of which *M.bovis* positive)	**20**	1	2	4	2	3		6	2
	Mammary lymph nodes	**74**	23	12	6	3	9	8	11	2
	(of which *M.bovis* positive)	**48**	20	8	2	2	5	5	5	1

Notes:
1. Data only go back to the advent of the current TB Culture System at VLA. Prior to that tissues were not being recorded between 2000 and November 2003. 'Year' is the year processed at VLA.
2. Only sample references that appear in the VetNet database and thus enable retrieval of the animal's sex are included.
3. These figures only represent the animals sampled by AH or the MHS and submitted to VLA for examination and culture. In multiple-reactor breakdowns only a representative number of animals are sampled for culture (normally up to 3 reactors with visible lesions). Less animals per breakdown have been submitted since 2009.
4. 'NVL' = no visible lesions of TB, 'VL' = typical visible lesions of TB recorded.
5. One VL animal may present with multiple TB lesions and thus have several tissues recorded against it.

Annex 5

Terminology related to the assessed level of risk

For the purposes of this risk assessment the terminology adopted by OIE* and EFSA* will be used to describe the assessed level of risk.

Category	Interpretation
Negligible	Event is so rare that it does not merit to be considered
Very low	Event is very rare but cannot be excluded
Low	Event is rare but does occur
Medium	Event occurs regularly
High	Event occurs very often
Very high	Event occurs almost certainly

*OIE (2004). Handbook on Import Risk Analysis for Animals and Animal Products. Volume 1, World Organisation for Animal Health.

*EFSA (2006) Scientific report on migratory birds and their possible role in the spread of highly pathogenic avian influenza. EFSA journal 357, 1-46.