INTRODUCTION

1. This is the first of a two-part assessment of the possible health risks to consumers associated with Mycobacterium bovis and milk and milk products.

2. The purpose of this paper is to:
   - Seek the views of members on 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.

3. Part II will address the risks from unpasteurised milk and milk products and will be presented to ACMSF in 2011, once the results of the research on the survival of M. bovis in unpasteurised milk cheeses are available.

BACKGROUND

4. In autumn 2009, the FSA Board requested that the Agency review the potential risks to consumers of meat and milk from cattle with evidence of M. bovis infection. The request was made as a number of years have passed since the ACMSF last considered the issue in 2001 and since that time the incidence of M. bovis infection in the UK cattle population has increased. The Board would like reassurance that the current controls on meat and dairy products are adequate to protect human health given this rise.

5. 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.

6. In its 2002 Report on M. bovis, the Committee 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. In light of the FSA Boards' request that the Agency re-consider the risks to consumers from milk and milk products, this briefing paper has been prepared to assist the Committee to assess the potential for pasteurised milk and milk products contaminated with M. bovis to enter the food chain and whether this risk has changed in light of the increase in M. bovis infection in cattle in the UK.
7. The risks associated with unpasteurised milk and milk products will be addressed in 2011, when the results become available from an on-going FSA funded research project on the survival of *M. bovis* in unpasteurised milk cheeses. Once the risk assessments are complete, the results will be presented to the FSA Board.

The potential for *M. bovis* to be present in unpasteurised cows’ milk

8. The discussion below outlines the main components of the bovine TB control programme in the UK and the potential for *M. bovis* to be present in unpasteurised cow’s milk destined for the food chain.

9. The current bovine TB control programme in the UK is designed to quickly detect and remove *M. bovis* infection in the national cattle herd and prevent it from spreading into low incidence areas. This is achieved mainly by routine testing of herds, slaughterhouse inspection of cattle carcases, targeted testing of herds and animals at risk and restrictions on the movements of infected herds and high risk cattle.

10. The cornerstone of the bovine TB surveillance and control programme is the routine tuberculin skin testing of cattle herds performed according to a frequency (annual to 4-yearly) dictated by the local incidence of TB herd breakdowns. All cattle 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 markedly increased at the beginning of 2010 relative to previous years. As a result of this change, 45.5% of all English cattle herds are now annually tested.

11. If TB is detected in a herd, either by use of the skin test or through slaughterhouse surveillance, the herd will lose OTF status. All positive skin test reactors and any at risk contacts are required to be isolated and are compulsorily removed and slaughtered by Animal Health 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 status. 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 cattle takes place very occasionally. For milk that is consumed unpasteurised, 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. there is no evidence of *M. bovis* infection. 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), Animal Health will immediately notify the relevant Local Food Authority and DARD will notify the relevant human health authorities. Milk from animals giving a positive reaction to the tuberculin test (or gamma-interferon 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 the OTF status is restored. The control programme in Northern Ireland works on broadly similar principles.

12. There are two aspects of the biology of TB infection in cattle that need to be understood when considering the likelihood that unpasteurised milk destined for the food chain might contain *M. bovis*. The first is the route by which milk could become contaminated with *M. bovis* and the occurrence of tuberculous mastitis. The second is the potential for undiagnosed but infected cows to remain in a herd so that their milk continues to enter the food chain.

13. Where there is infection in the dairy 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 this can occur before clinical signs of infection are apparent, this is rare. Contamination of the milk is most likely to occur when infection becomes disseminated and where this results in tuberculous mastitis. In such cases large numbers of bacteria can be shed in the milk. However, evidence shows that such cases are rare in the UK.

14. In 1934, before the adoption of milk pasteurisation and compulsory tuberculin skin testing of cattle, it was reported that more than 40% of dairy cows in Great Britain were infected with *M. bovis* and 0.5% suffered from TB of the udder. Despite the resurgence of bovine TB in the cattle population since the late 1980s, the percentage of animals (and therefore dairy cows) infected remains much lower than it was in the 1930s. Nowadays tuberculous mastitis is rarely seen in cows in the UK. 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. 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 is very small (<1%) (see Annex 1). However, these figures probably represent an underestimate of the true prevalence of udder lesions, since it is quite possible that the udder and associated lymph nodes of TB reactors and other TB suspect animals do not receive the same degree of attention during post-mortem inspection at the abattoir as other organs more typically affected with TB, such as the lungs and lymph nodes of the head and thoracic cavity.

15. Thus it is not possible with the data currently available to accurately estimate the frequency with which *M. bovis* is shed in infected cows’ milk in the UK (and whether there has been an upward or downward trend in recent years), but it is somewhat reassuring to note that only a handful of incidents of TB in dairy calves associated with exposure to contaminated milk from tuberculous cows are reported by Animal Health every year. Some of those unusual incidents of TB mastitis have been documented in the veterinary literature and, although few herds are affected every year, the animal prevalence within those herds can on occasions be high, with large numbers of calves infected by a single tuberculous cow depending on the calf feeding system used on the farm (Monies and Head 1999, Houlihan et al. 2008).

16. On the second point, there is the potential for animals that are infected with *M. bovis* to go undetected by the skin test for some time and therefore for their milk
to continue to enter the food supply. The tuberculin skin test used in the UK is approximately 80% sensitive and in recognition of this, the test is often used serially and is supported by other diagnostic methods. In addition, there are a range of reasons why an infected animal may fail to react to the skin test. These include a poor skin testing technique, use of tuberculin of reduced potency, desensitisation after injection of tuberculin, immunosuppression during early post-partum, the administration of certain drugs or co-infections with certain parasites and viruses. A substantial proportion of those infected animals missed by the skin test (false negatives) will be detected by the more sensitive gamma interferon blood test, which is used in the UK TB control programme as a supplementary parallel test in some cattle herds with culture-confirmed *M. bovis* infection. Since the rollout of this test in Great Britain in October 2006 until 30 June 2010, 91,191 skin test-negative cattle have been gamma interferon tested, of which 11,114 proved positive and about 11% of those had visible pathological lesions of TB at post mortem examination. Cows may also be anergic i.e. have visible evidence of TB at slaughter but fail to show a cutaneous response to tuberculin (see Annex 2).

17. In summary, the potential for *M. bovis* to be present in unpasteurised milk destined for human consumption, either as drinking milk or processed dairy products, is minimised through frequent TB testing and removal of infected cattle and exclusion of reactor milk from the food chain. The risk cannot be totally eliminated as bovine TB screening tests are not fully sensitive and cattle can become infected between tests. Milk from anergic cattle, which go undetected by the skin test, may also enter the food supply. However, tuberculosis mastitis with shedding of bacteria into the milk is rare and, even if such cases are not recognised through TB testing or clinical examination, in intensively managed dairy herds infection will eventually lead to culling of the affected cow as an animal with a chronic mastitis problem that fails to respond to the conventional antibiotic therapy. The vast majority of milk is treated with pasteurisation before drinking or further processing and the effectiveness of pasteurisation in removing any bacteria is discussed below.

The potential for *M. bovis* to be present in unpasteurised milk from non-bovine species

18. Sporadic incidents of TB caused by *M. bovis* arise in non-bovine species (sheep and goats) and occur almost invariably in areas sustaining an endemic high incidence of TB in cattle. In GB, when a culture-confirmed episode of *M. bovis* infection is disclosed in farmed animals other than cattle, statutory movement restrictions are immediately applied on the herd/flock of origin and a veterinary risk assessment of the premises is carried out by AH. As with all confirmed incidents of *M. bovis* in cattle, AH 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 are usually lifted only once the affected herd or epidemiological group have been removed and slaughtered and after any tuberculin skin testing has been completed with satisfactory results, i.e. no reactor animals left on the premises. Ante-mortem TB testing of these species and removal of test reactors is voluntary.
19. 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.

20. 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. Currently Animal Health will test goats for TB whenever *M. bovis* infection is found in a co-located cattle herd. A control plan for the TB testing of sheep and goats is under development for the UK and controls on milk from affected herds are under consideration.

The potential for *M. bovis* to survive pasteurisation

21. Pasteurisation is the main critical control point in the processing of raw milk and it has a long history of application as a means of destroying any pathogenic bacteria which may be present.

Development of pasteurisation standards

22. Pasteurisation was first developed as a process to heat treat milk at the beginning of the 20th century. Early work showed Mycobacteria to be the most heat resistant of the pathogenic organisms found in milk. This, plus the acknowledged risk of humans catching tuberculosis from drinking raw milk, led to the destruction of *M. tuberculosis* being used as the basis for setting minimum pasteurisation standards.

23. In 1911, a minimum time/temperature for pasteurisation was set by the National Milk Standards Committee in USA, 62.8°C for 30 mins, known as the batch or holder method. The first official standard came in 1924 in the US when the First Pasteurised Milk Ordnance was published specifying a minimum of 61.1°C for 30 minutes. This was later followed in 1933 by the first standard for High Temperature Short Time pasteurisation (HTST) of 71.7°C for 15 seconds. A further change to the batch or holder method came in the 1950’s when the standard was increased to 62.8°C for 30 minutes to ensure destruction (at least a 5 log reduction in whole milk) of *Coxiella burnetti*, the cause of Q fever.

24. Apart from some rounding up of numbers to take into account Fahrenheit-Celsius conversions the above standards have remained unchanged to this day. The Codex Alimentarius Commission Code of Hygienic Practice for Milk and Milk Products specifies the minimum time/temperature combinations for batch and HTST pasteurisation as 63°C for 30 mins and 72°C for 15 secs respectively.

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1 *M. bovis* was only officially assigned that name in 1970. From 1934 onwards it was known as *M. tuberculosis* var. bovis so it is likely that in at least some of the reported studies on *M. tuberculosis*, the test organism would have been now classified as *M. bovis*. 
Current pasteurisation standards

25. Current legislative limits, in line with those specified by Codex, are set out in Regulation (EC) No 853/2004. The majority of dairy processors in the UK apply HTST heat treatment but batch pasteurisation is used by some smaller processors. Verification that pasteurisation has been carried out correctly is through testing the product for alkaline phosphatase activity. Alkaline phosphatase is an enzyme naturally present in raw milk which is destroyed by pasteurisation. A limit for the amount of ALP which may be present in pasteurised milk is specified for cows’ milk (350 mU/l) but not other species.  

26. The time/temperatures specified in the hygiene legislation are the minimum required and in practice the industry can and does apply higher temperatures and/or longer times. This may be to increase the shelf life of the milk or as a precaution against Mycobacterium avium subspecies paratuberculosis (MAP). However, if the time and/or temperature are increased too much undesirable organoleptic changes are detectable.

27. The legislation specifies that pasteurisation should be achieved by HTST or batch pasteurisation or any other combination of time/temperature conditions to obtain an equivalent effect. Milk products with a higher fat content than milk, or a higher sugar content or viscosity, will require pasteurisation conditions in excess of those for milk to achieve destruction of all pathogens. For instance, cream requires a minimum of 75°C for 15 seconds.

Evidence for the efficacy of pasteurisation

28. As has been described, the minimum time/temperature combinations for pasteurisation set down in the food hygiene legislation were established over 50 years ago and are based on a body of scientific evidence built up over the previous 50 years.

29. A key review of the scientific evidence for the thermal destruction of *M. tuberculosis* was published in 1927 by North and Park, which supported the standard set in 1924 in the First Pasteurised Milk Ordnance (61.1°C for 30 mins) as providing an ample safety margin. Through the production of a thermal death curve it was concluded that a heat treatment of 62.2°C for 30 minutes would ensure a margin of safety for the destruction of *M. tuberculosis* of 20 minutes or 3.3°C.

30. As plate heat exchangers were developed in the 1930’s, further studies on thermal destruction were carried out. Dahlberg (1932) conducted a review of the

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2 Raw milk from different species contains different levels of alkaline phosphatase.

3 MAP has been proposed as the cause of Crohn’s disease in humans but a link has not been demonstrated. Pasteurisation has been shown to be very effective at destroying MAP but no single intervention is currently guaranteed to eliminate it completely. Dairy industry guidance to Good Hygiene Practice (currently out to consultation) recommends at least 72°C for 25s. However, the FSA concluded in 2002 that the weight of evidence was against there being any demonstrable benefit in increasing pasteurisation holding times to 25 seconds if the aim is total elimination of MAP from drinking milk.
research which led to the HTST standard of 71.7°C for 15 secs being included in
the 1933 edition of the US Public Health Service Milk Ordnance and Code.

31. Further work was carried out on the heat resistance of both *M. tuberculosis* and
*M. bovis* in the following 30 years, which led to the common acceptance that the
standards established for batch and HTST pasteurisation were adequate to
destroy both these Mycobacteria.

32. A key piece of work by Kells and Lear (1960) was specifically aimed at examining
the heat resistance of three strains of *M. bovis* in milk using laboratory scale
batch pasteurisation and 10^4 or 10^6 cfu/ml. The z values obtained ranged from
4.8°C to 5.2°C and showed that the time and temperature required to inactivate
*M. bovis* were much lower than reported by Dahlberg, on which the standards
were based. It was estimated that the pasteurisation standards provided a safety
margin of about 28.5 minutes at 61.7°C and about 14 secs at 71.7°C.

33. More recent evidence of thermal inactivation of *M. bovis* in whole milk at 63.5°C
was produced by Grant (1996). Survivors were enumerated after heating for 0, 5,
10, 15, 20 and 30 min and thermal death curves were constructed. *M. bovis* was
found to exhibit a linear thermal death curve and there was no survival after
heating at 63.5°C for 30 min. A high inoculum level (10^7 cfu/ml) was used to
represent a worst case scenario. Should a cow excrete organisms into the milk at
this level there would be an initial dilution with milk from the rest of the herd then,
in most cases, considerable further dilution at the dairy before the milk was
pasteurised.

**Microfiltration of milk**

34. Microfiltration of milk is used in the dairy industry to produce milk with an
extended shelf life, greater than that achieved by pasteurisation alone. The milk
is separated into skimmed milk and cream, then the skimmed milk is subject to
microfiltration (typically 1.4 µm pore size) to remove bacteria and the cream is
heat treated, before the skimmed milk and cream are recombined and
pasteurised. *M. bovis* is a relatively large bacterium (2 – 4 µm long, 0.2 – 0.5 µm
wide) and would be expected to be removed by microfiltration. As microfiltered
milk is always pasteurised as well, the process will not be explored further in this
paper.

**Human cases of *M. bovis* linked to milk consumption**

35. In the early part of the 20th century, an estimated 40% of dairy herds were
infected with *M. bovis* and the primary route of infection for humans was
unpasteurised milk. In 1934 it was estimated that some 2,500 people, principally
children, died annually from TB due to *M. bovis* and 50,000 people were
contracting the disease. The introduction of a compulsory eradication programme
in 1950 and the increasing pasteurisation of milk led to a dramatic reduction in
the level of human disease.

36. Over the last 15 years, despite a rise in TB in cattle, only a very small proportion
of human TB cases each year (approximately 30 or <1%) have been due to *M.
bovis* and the vast majority have been caused by *M. tuberculosis*. 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 *M. bovis* was more prevalent in the UK cattle population 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 small number of human cases attributed to direct occupational contact with infected animals have also occurred. There is no evidence that these infections have been acquired through recent consumption of contaminated meat or dairy products derived from *M. bovis* infected animals in the UK.

**Summary**

37. The potential exists for *M. bovis* to be present in raw cows’ milk. The main risk arises from direct contamination of the milk in the udder, which is most likely when infection becomes disseminated and there is tuberculous mastitis. However, despite the resurgence of bovine TB since the late 1980’s, tuberculous mastitis is rarely seen in cows in the UK as the surveillance programme means that infected animals are removed from the herd in the early stages of infection. Anergic animals, which are infected but do not react to the tuberculin skin test, may be detected through use of the gamma interferon test or, in exceptional circumstances, a serological test. Controls which further minimise the risk do not allow milk from reactor animals to enter the food chain and all milk from herds which have lost their OTF status must be pasteurised. The TB controls on non-bovine dairy species (sheep and goats) are less stringent but incidents of *M. bovis* infection in these species are only sporadic.

38. There is a significant body of evidence to show that, if carried out correctly and at the time/temperatures required in the food hygiene legislation, *M. bovis* is destroyed by both batch and HTST pasteurisation and that there is an adequate safety margin. This is supported by the very low and stable level of human *M. bovis* infections seen in the UK for the last 15 years (<1% of culture confirmed cases) and there is no evidence that these infections have been acquired through recent consumption of contaminated milk.

**ACMSF action:**

39. The ACMSF is requested to consider 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.

Secretariat
September 2010
References


North CE and Park WH (1927) Standards for milk pasteurisation. Amer. J. Hyg. 7, 147-154

Dahlberg AC (1932) The margin of safety between the thermal death point of the tubercle bacillus and the thermal cream layer volume impairment in pasteurising milk at various temperatures. New York State Agricultural Experiment Station, Technical Bulletin No. 303

Kells HR and Lear SA (1960) Thermal death time curve of Mycobacterium tuberculosis var. bovis in milk. J. Food Prot. 61, 974 - 978

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

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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.
4. 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.
5. ‘NVL’ = no visible lesions of TB, ‘VL’ = typical visible lesions of TB recorded.
6. One VL animal may present with multiple TB lesions and thus have several tissues recorded against it.
Anergic Cattle

A small subset of false negative cattle are those that present with disseminated TB pathology (and possibly clinical signs of TB) at slaughter and yet fail to react to the tuberculin test. This is believed to be 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, known as ‘anergic animals’, the cell-mediated immune response measured by the skin and gamma-interferon tests is gradually replaced by circulating antibodies against *M. bovis*. Ante-mortem identification of such animals requires a different type of immunological test (so-called serological TB assays).

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. In general, it is believed that those cases are quite rare and seldom arise on their own (i.e. the OTF status of the herd will already be suspended following the identification of other infected animals as reactors). Animal Health will use serological tests very sparingly and only when there is evidence of cattle-to-cattle spread in a chronically infected herd despite the repeated application of the tuberculin and gamma-interferon tests. Likewise, antibody assay may be used in NI where considered beneficial for disease control in a herd, but this is infrequent.