



**RISK PROFILE:
MYCOBACTERIUM BOVIS IN MILK**

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RISK PROFILE:
***MYCOBACTERIUM BOVIS* IN MILK**

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1 EXECUTIVE SUMMARY

The purpose of a Risk Profile is to provide contextual and background information relevant to a food/hazard combination so that risk managers can make decisions and, if necessary, take further action. Risk Profiles include elements of a qualitative risk assessment, as well as providing information relevant to risk management. Risk profiling may result in a range of activities e.g. immediate risk management action, a decision to conduct a quantitative risk assessment, or a programme to gather more data. Risk Profiles also provide information for ranking of food safety issues.

Tuberculosis (Tb) is most commonly caused by *Mycobacterium tuberculosis*, but a proportion of human cases are caused by *Mycobacterium bovis*. The notified incidence of tuberculosis in New Zealand in 2007 (including reactivations) was 6.9 per 100,000 population. The proportion of total tuberculosis cases in recent years estimated to be caused by *M. bovis* in New Zealand (1-3%) is similar to other developed countries.

The dose response relationship for ingestion of *M. bovis* is unclear, but risk of infection via ingestion appears to be markedly lower than for inhalation from aerosols produced by infected animals.

If it is assumed that approximately 3% of all notified cases of tuberculosis in New Zealand are caused by infection with *M. bovis*, then the current incidence of tuberculosis caused by this organism is approximately 0.1-0.3 per 100,000. However there is no conclusive evidence that these infections are caused by transmission in milk. Given that pulmonary infections are at least as prevalent as extra-pulmonary infections, acquisition of infection by inhalation rather than ingestion of food appears to be important, possibly via occupational contact with infected animals.

Unpasteurised milk used to be a common vehicle for transmission of *M. bovis*. However, since the introduction of mandatory pasteurisation, milk has largely ceased to be a vehicle. Since 1995, two cases of *M. bovis* infection in New Zealand have reported consuming unpasteurised milk among the risk factors recorded, but in neither case was this vehicle confirmed.

Pasteurisation is sufficient to control *M. bovis* in milk. There is likely to be some consumption of unpasteurised milk on New Zealand farms and from sales of milk at a few farm gates. A recent study of transmission of *Campylobacter* in a semi-rural community found that consumption of unpasteurised milk was not uncommon, with 20% of respondents reporting consumption of unpasteurised milk (Baker *et al.*, 2002). However, as a proportion of total national milk consumption this amount is likely to be very low. The majority of New Zealand dairy cattle are tested annually, and these show a very low prevalence of bovine tuberculosis, meaning that the risk from unpasteurised milk will also be low.

Active risk management for *M. bovis* in milk in New Zealand includes:

- Cattle and deer herd monitoring and active measures to eradicate Tb from all breakdown herds;
- Mandatory pasteurisation of milk (with an exception for sales of up to 5 litres at the farm gate); and,

- Vector control measures (especially brush-tailed possum and ferret control), which markedly reduces the incidence of *M. bovis* infection in cattle and deer.

The New Zealand Food Safety Authority is currently considering a proposed framework for the manufacture, importation and sale of raw milk products in New Zealand (Discussion Document 04/08). This is concurrent with similar considerations by Food Standards Australia New Zealand for Australia (Proposal P1007).

In this context, it is relevant to consider the potential risk from *M. bovis* in milk, should the requirement for mandatory pasteurisation be removed. It is assumed that Animal Health Board controls on bovine tuberculosis would be maintained at their current level. In this scenario the risk from *M. bovis* in raw milk is considered to remain low due to the low prevalence in cattle as demonstrated by the Animal Health Board testing, and the indications that the dose-response relationship for ingestion is markedly lower than for the respiratory route. However, due to the potential for mixing of milk during distribution, consideration could be given to instituting additional controls on raw milk and raw milk products from positive dairy herds, and in areas where *M. bovis* infection in wildlife reservoirs is endemic.

The data gaps identified in this Risk Profile are:

- Prevalence (if any) of *M. bovis* in the raw milk of infected animals detected by Animal Health Board testing;
- Tuberculosis status of milking goats in New Zealand, and production of goats milk for consumption; and,
- Dose response relationship for *M. bovis* infection in humans via the gastrointestinal route.

2 STATEMENT OF PURPOSE

The purpose of a Risk Profile is to provide contextual and background information relevant to a food/hazard combination so that risk managers can make decisions and, if necessary, take further action. Risk Profiles are part of the Risk Management Framework (RMF) (<http://www.nzfsa.govt.nz/about-us/risk-management-framework/index.htm>) approach taken by the New Zealand Food Safety Authority (NZFSA). The Framework consists of a four step process, as shown in Figure 1.

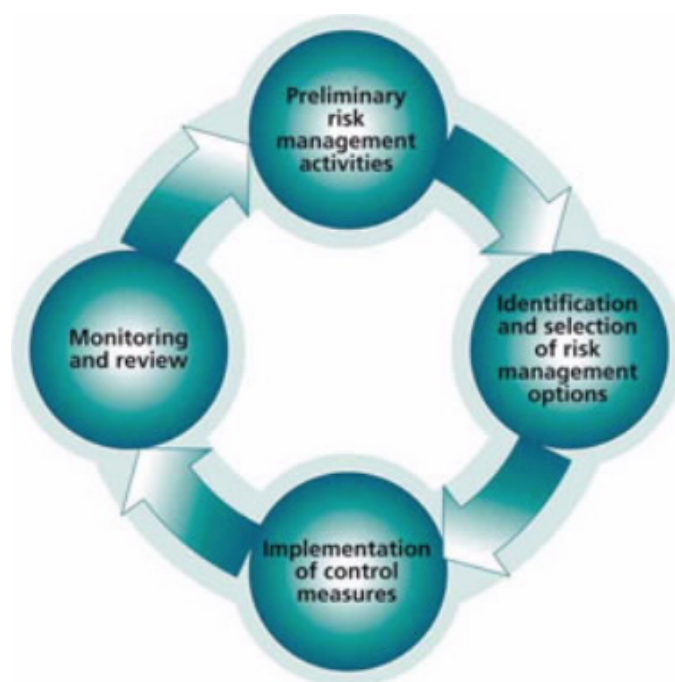


Figure 1: The four steps of the Risk Management Framework

This initial step in the RMF, Preliminary Risk Management Activities, includes a number of tasks:

- identification of food safety issues
- risk profiling
- establishing broad risk management goals
- deciding on the need for a risk assessment
- if needed, setting risk assessment policy and commissioning of the risk assessment
- considering the results of the risk assessment
- ranking and prioritisation of the food safety issue for risk management action.

Risk profiling may be used directly by risk managers to guide identification and selection of risk management options, for example where:

- rapid action is needed
- there is sufficient scientific information for action
- embarking on a risk assessment is impractical.

2.1 Food/hazard combination and risk management questions

The food/hazard combination addressed by this Risk Profile is *Mycobacterium bovis* in milk.

New Zealand Food Safety Authority is currently considering a proposed framework for the manufacture, importation and sale of raw milk products in New Zealand (Discussion Document 04/08). This is concurrent with similar considerations by Food Standards Australia New Zealand for Australia (Proposal P1007). In this context, it is relevant to understand the risk from *M. bovis* in milk, should the requirement for mandatory pasteurisation be removed.

The NZFSA have commissioned this Risk Profile to address the following specific risk management questions:

- What evidence is available to demonstrate the current low level of risk for this food/hazard combination?
- If the current risk management measures were changed or removed, how would the characterisation of the risk change?

3 HAZARD AND FOOD

3.1 *Mycobacterium bovis*

The information in this section represents a summary of a microbiological data sheet relevant to this Risk Profile. Further details are presented in Appendix 1. These data sheets are prepared for the NZFSA by ESR, and a full set can be found at: <http://www.nzfsa.govt.nz/science/data-sheets/index.htm>.

Mycobacterium bovis is a member of the “*Mycobacterium tuberculosis* complex” (MTBC), a group of genetically similar organisms which infect humans and animals. MTBC includes five named ‘species’ (*M. tuberculosis*, *M. bovis*, *M. africanum*, *M. canetti* and *M. microti*) and several variants whose taxonomy is still under debate (Rastogi *et al.*, 2001; Brosch *et al.*, 2002).

Unlike *M. tuberculosis* which (in all but exceptional circumstances) only infects humans, *M. bovis* has a broad host range and is the principal agent responsible for tuberculosis in domestic and wild mammals, including cattle. Infection can potentially be spread to humans via contaminated milk or meat, or directly by inhalation of aerosols from infected animals or carcasses.

Characteristics of the “tuberculosis complex” that distinguish them from other *Mycobacteria* include slow growth; a minimum growth temperature of approximately 30°C is reported for *M. tuberculosis* (Spahr and Url, 1994). Given the short shelf life of foods that it has been associated with, e.g. unpasteurised milk and raw meat, growth in foods is unlikely to be significant. The organism is inactivated by normal pasteurisation.

Typing schemes so far developed for *M. bovis* are useful for epidemiological investigations, but do not allow discrimination in relation to virulence or host specificity. More detailed information on typing schemes is presented in Appendix 2.

3.2 Sources of *Mycobacterium bovis*

Environment: Can persist and remain infective in the environment for long periods.

Animal: Many domestic and wild animals have been found to be infected with *M. bovis*. Some are reservoirs of infection or “maintenance hosts” in which infection is self sustaining from generation to generation. These species include farmed and wild cattle, deer, and goats, feral pigs, ferrets, and possums in New Zealand, and Eurasian badgers in the UK. In a number of countries, the failure to eradicate *M. bovis* from cattle is due to the presence of a wildlife reservoir (de Lisle *et al.*, 2001). Direct transmission from animals to humans may occur via aerosols.

Human: In the absence of immunosuppression, person to person transmission of tuberculosis caused by *M. bovis* occurs very rarely (Grange, 2001; Evans *et al.*, 2007).

Food: Meat and milk derived from infected animals may contain the organism. Lesions in skeletal muscle are very rare and observed only in animals with advanced infection.

Contamination of milk occurs via tuberculous lesions in the udder and associated lymph nodes.

Transmission Routes: Prior to the widespread adoption of pasteurisation, the major *M. bovis* pathway from cattle to humans was via contaminated milk. While transmission by meat derived from infected animals is theoretically possible, no cases have been documented and the risk is believed to be small (see Risk Profile for *M. bovis* in red meat: http://www.nzfsa.govt.nz/science/risk-profiles/FW0320_Mbovis_in_meat_final_May_2006.pdf and the UK Ministry of Agriculture, Fisheries and Food website <http://www.maff.gov.uk/animal/tb/point1/point1.shtml>).

3.3 The Food Supply in New Zealand: Milk

Supplemental information on milk in New Zealand is given in Appendix 1.

Milk is defined by Codex as “the normal mammary secretion of milking animals obtained from one or more milkings without either addition to it or extraction from it, intended for consumption as liquid milk or for further processing” (Codex, 1999). Raw milk has been defined as “milk which has not been heated beyond 40°C or undergone any treatment that has an equivalent effect” (Codex, 1999; 2004).

3.3.1 Milk production in New Zealand

The historical and projected numbers of dairy cattle and production of liquid milk for New Zealand are shown in Table 1 (MAF, 2007). Total dairy cow numbers were obtained from Statistics New Zealand (2007a).

New Zealand is the eighth largest producer of milk in the world, accounting for 2.2% of total world milk production and exports the vast majority of its dairy products to 152 countries (MAF, 2007). The domestic milk market is estimated at 386 million litres per annum (approximately 0.4 million tonnes) (Diane Schumacher, NZFSA, Personal communication, April 2007).

The Waikato province has the highest number of dairy cattle at 1.7 million. However, the greatest change in numbers recently has occurred in Canterbury, increasing from 605,000 in 2005 to 656,000 in 2006. The South Island herd has increased from 225,000 in 1981 (8 % of the national dairy herd) to 1.5 million (28 %) in 2006. Dairy cattle numbers have risen from 2.9 million in 1981 to 5.2 million in 2006 (Statistics New Zealand, 2007b).

Table 1: Number of dairy cattle and production of liquid milk for New Zealand, 2005-2011

	Actual			Forecast			
Year (to May)	2005	2006	2007	2008	2009	2010	2011
Livestock numbers (millions)							
Cows and heifers in calf or in milk	4.10	4.12	4.14	4.23	4.35	4.45	4.54
Total dairy cattle	5.09	5.17	5.40	5.41	5.43	5.48	
Production (million tonnes)							
Liquid milk*	14.14	14.80	15.31	15.57	16.13	16.70	17.32

* Figures for liquid milk production calculated from SONZAF website milk solid figures, using the conversion factor of 8.58% (<http://www.maf.govt.nz/mafnet/rural-nz/statistics-and-forecasts/sonzaf/2007/index.htm>).

Goats are reported as also being susceptible to *M. bovis* infection and can develop both pulmonary tuberculosis and mastitis, with shedding into milk (O'Reilly and Daborn, 1995). In 1999 there were an estimated 187,000 goats in New Zealand, but the proportion of these which were dairy goats was unknown. Approximately 80 commercial herds (average herd size 260 milking does) were registered with the Dairy Goat Cooperative at that time. Most of the product is reported to be exported but there is also a small local market for cheese and milk (Jackson and King, 2002).

3.3.2 Imported food

Imported milk is not significant in the food supply. According to data from Statistics New Zealand, in the 12 months to September 2007, only a small amount (6,500 litres) of fresh milk and cream was imported from Australia and the Netherlands (the pasteurisation status of this material is unclear from the import descriptors, but presumably any such products are subject to the same pasteurisation requirements as domestic production). No imports were reported under this category in the year to September 2008. Approximately 1,800 tonnes of milk and cream "other than fresh" was also imported from Australia; this will include "ultra-heat-treated" (UHT) products.

3.3.3 *M. bovis* in milk

Bovine tuberculosis primarily affects the upper (tonsils and draining lymph nodes) and lower (lungs and draining lymph nodes) respiratory tract, and intestinal tract (ileo-jejunum and draining nodes) of cattle. Only approximately 1% of animals suffer from infected udders (mastitis) (Collins, 2000). *M. bovis* cells are shed in large numbers directly from infected mammary tissue into the milk.

Since milk has an almost neutral pH (6.7), a high water content and a variety of nutrients, it represents an ideal substrate for microbial growth. However, this is unlikely to be important for *M. bovis* as it is very slow growing. A minimum growth temperature of approximately 30°C is reported for *M. tuberculosis* (Spahr and Url, 1994).

Shedding of *M. bovis* by an infected animal in oral and respiratory secretions and in the faeces can occur before a clinical diagnosis is made, and cross-contamination of the expressed milk from these animals may also occur (European Scientific Panel on Biological Hazards, 2003).

3.4 Inactivation of *Mycobacterium bovis* in milk

Exposure to the organism via milk appears to be the only significant foodborne exposure (O'Reilly and Daborn, 1995; Cousins and Dawson, 1999). *M. bovis* infection was a significant public health problem prior to the introduction of pasteurisation of milk and milk products but cases now are rare (ESR, 2008).

The time-temperature combination necessary for the destruction of *M. tuberculosis* was the prime factor in the establishment of milk pasteurisation standards, as it was considered the most heat resistant of the pathogens likely to be present in milk (Grant *et al.*, 1996). The most commonly used standards are the low temperature long time (LTLT) (63.5°C for 30 minutes) method, and the high temperature short time (HTST) method (71.7°C for 15 seconds).

These Standards provide considerable safety margins over the time required for the destruction of *M. bovis*; the margins are 28.5 minutes for the low temperature long time method, and 14 seconds for the high temperature short time method (Kells and Lear, 1960). This assumes that the maximum concentration likely to occur in milk is 10^4 /ml (Kells and Lear, 1960). These authors also provided data that when extrapolated, and assuming linearity in the kill curve, the D time at 72°C should be in the order of 0.15 second (in microbiological terms, "D" refers to a 90% (or decimal or 1 log cycle) reduction in the number of organisms). *M. bovis* inoculated at 10^5 cfu/ml was not able to be recovered from milk samples after pasteurisation by heating to 63.5°C for 20 minutes (Grant *et al.*, 1996).

3.5 Exposure Assessment

3.5.1 The Hazard in the New Zealand Food Supply:

The prevalence of *M. bovis* in raw milk in New Zealand depends on:

- The prevalence of *M. bovis* infection in dairy cattle; and,
- The spread of bacteria from the primary and secondary sites of infection (complexes), which are principally located in the lymph nodes, into mammary tissue (milk).

A national tuberculosis control programme, of varying intensities, for cattle and deer has operated in New Zealand for over 70 years. Currently this is managed by the Animal Health Board (AHB). Under the Biosecurity Act, the AHB has developed and implemented the national 'Bovine Tuberculosis Pest Management Strategy (PMS)' (see <http://www.ahb.org.nz/AHBWebsite>). The main PMS objective is to reduce the prevalence of infected cattle and deer herds to a maximum of 0.2% by 2013. This is one aspect of the World Animal Health Organization's (OIE) standard for 'country freedom' from bovine tuberculosis.

Operationally there are two key inter-related elements of the control programme; elimination of Tb-infected wildlife (mainly possums) and disease control activities in cattle and deer herds. The latter involves on-going surveillance for infection (periodic testing and abattoir examination), rapid eradication of infection from herds, and movement control (to stop the spread of infection between herds).

In animals, as in humans, pre-clinical infection is initially determined by use of the primary tuberculin test. This test is based on detection of the specific immunological response to infection, and involves intradermal injection of protein antigens derived from *M. bovis* (purified protein derivative, PPD) and inspection three days later for evidence of a local inflammatory reaction at the site of injection. A small proportion of primary test positive animals (“reactors”) are slaughtered. For the remaining animals other ancillary tests of cellular and humoral immunity are conducted and positive animals in these tests are also slaughtered (AHB, 2007).

In the year to June 2007, 3.09 million primary tuberculin tests were performed on dairy cattle; representing approximately 57% of the 5.40 million dairy cattle in New Zealand. At 30 June 2007 there were 130 (0.18%) infected cattle herds (5,718 animals), compared to 364 infected herds in the year to June 2002. Of these 130 infected herds in 2007, 55 (42%) were dairy herds (AHB, 2002; 2007).

M. bovis has been cultured from tuberculous lesions in feral goats and “occasional” dairy goats originating from areas in New Zealand where the infection is known to be endemic in possums (Thompson, 2001).

No surveys or other data on the prevalence of *M. bovis* in milk in New Zealand have been located.

3.5.2 Food Consumption: Milk

3.5.2.1 *Raw milk consumption*

Apart from limited farm-gate sales of raw milk, pasteurisation is mandatory for dairy products from milking animals (cows, sheep, goats) for human consumption in New Zealand, and data on raw milk consumption in New Zealand are very limited. No record of raw milk consumption could be identified in the results of the 1997 National Nutrition Survey (Russell *et al.*, 1999) or the 2002 National Children’s Nutrition Survey (Ministry of Health, 2003).

There are some studies that provide indirect information regarding consumption of unpasteurised milk in New Zealand. Wickens *et al.* (2002) surveyed 293 New Zealand children in the age range 7-10 for risk factors associated with allergic diseases. In response to questions as to whether they had ever consumed unpasteurised milk during the first two years of life (answers provided by parents), 23% of children currently living on farms responded positively, while only 8% of non-farm children responded positively. Consumption of unpasteurised milk was reported by 9 of 44 cases (20%) interviewed for a campylobacteriosis transmission routes study amongst a predominantly rural population in Ashburton (Baker *et al.*, 2002). Consumption of unpasteurised milk was reported by 5.8% of cases and 2.4% of controls in the primarily urban case control study (Eberhart-Philips *et al.*, 1997).

According to Statistics New Zealand there were 11,400 dairy farms in New Zealand at June 2007.

In the United States unpasteurised milk consumption has been estimated as 0.5% of total milk consumption (FDA, FSIS, 2003). In England and Wales, the Dairy Hygiene

Inspectorate has estimated that only 0.01% of cows' milk is consumed raw (Food Standards Agency, 2005).

3.5.2.2 *Total milk consumption*

The per capita consumption of milk in New Zealand increased from 1942, when subsidies were first placed on milk, to a peak in 1973. Subsidies were removed in 1985 and per capita consumption has been decreasing steadily since 1976 (Wham and Worsley, 2001). It has been estimated that the New Zealand liquid milk market is approximately 386 million litres per annum (Diane Schumacher, NZFSA, Personal communication, April 2007). This equates to approximately 90 litres/person per annum for the New Zealand population or 247 g/person/day. This represents the per capita amount of milk available for consumption.

Milk consumption data from New Zealand's nutrition surveys (Russell *et al.*, 1999; Ministry of Health, 2003) have been analysed (Cressey *et al.*, 2006a). Summary information is included in Table 2. 'Consumers' refers to those survey participants who reported consuming milk in the previous 24-hour period, while respondents refers to all survey participants.

Table 2: Summary of milk consumption by New Zealanders based on data from the 1997 National Nutrition Survey and the 2002 National Children's Nutrition Survey

Parameter	Age group		
	5-15 years*	15+ years#	65+ years#
Proportion of population consuming on any day	72.5%	87.7%	90.2%
Servings per consumer per day	1.7	3.7	4.1
Consumer mean intake (g/day)	271	272	244
Respondent mean intake (g/day)	197	239	220
Mean serving size (g)	157	73	60
Median serving size (g)	129	42	32
95 th percentile serving size (g)	335	258	206

* from 2002 National Children's Nutrition Survey (Ministry of Health, 2003)

from 1997 National Nutrition Survey (Russell *et al.*, 1997)

The difference in consumption patterns between adults and children reflects the fact that children primarily consume milk as a beverage on its own, while adults will often consume milk as an ingredient in tea or coffee.

Similar figures to these have been reported for Australia (Australian Bureau of Statistics, 1999), with the proportion of Australian children consuming 'dairy milk' declining from 90.0% for 2-3 year olds to 74.7% for 12-15 year olds, while 83.3% of adults 19 years and over and 86.7% of adults 65 years and over reported milk consumption. A slightly different pattern was seen for mean daily intakes for the Australian study, with mean daily intakes for children in the range 278 – 388 g/day, with adults 19+ years having a mean intake of 203.5 g/day and adults 65+ years having a mean intake of 197.7 g/day.

These figures are also reasonably consistent with the estimated average amount of pasteurized milk available for consumption in New Zealand (247 g/person/day).

The USA risk assessment for *Listeria monocytogenes* (FDA/FSIS, 2003) determined median serving sizes for pasteurised or unpasteurised milk as being 244 g/serving, with 75th, 95th and 99th percentile serving sizes of 245, 488 and 732 g/serving respectively. Analysis of the distribution of individual servings of milk reported in the 1997 NNS gives values of 42, 70, 258, 450 g/serving for the 50th, 75th, 95th, 99th percentile serving sizes. The large discrepancy between the USA and New Zealand situations is likely to be that the 1997 NNS included milk added to tea or coffee as a separate serving of milk, whereas it is likely that the USA situation only represents milk consumed as a beverage on its own.

3.5.3 Qualitative exposure assessment

3.5.3.1 *Number of servings of raw milk and serving size*

If it is assumed that pasteurisation in New Zealand is effective in eliminating *M. bovis*, then an exposure assessment is limited to raw milk consumption. As discussed earlier, there are insufficient data to estimate the prevalence of raw milk consumption in New Zealand. Serving size may be extrapolated from the serving sizes of pasteurised milk, discussed in section 3.5.2.2.

3.5.3.2 *Frequency of contamination*

Unknown, but likely to be very low given the low prevalence of infected dairy cows, as determined by control programmes.

3.5.3.3 *Predicted contamination level at retail*

Not known for New Zealand. Given the assumption made in the point above, the levels present are also likely to be very low.

3.5.3.4 *Growth rate during storage and most likely storage time*

The organism is very slow growing and is unlikely to increase significantly in numbers during the storage of raw milk.

3.5.3.5 *Heat treatment*

Not applicable.

3.5.3.6 *Exposure summary*

Although the number of servings of raw milk in New Zealand cannot be estimated, there are indications that up to 20% of the rural population, and up to 8% of the non-rural population have consumed raw milk at some time (see Section 3.5.2.1). Nevertheless, any exposure to *M. bovis* will be low, considering the low prevalence of infected dairy cows.

3.5.4 **Overseas Context**

No surveys or other data on the prevalence of *M. bovis* in the milk supply of other countries have been found.

4 EVALUATION OF ADVERSE HEALTH EFFECTS

Tuberculosis is the general name for a group of diseases associated with the presence of *Mycobacterium* spp. (MTBC), of which pulmonary (lung) tuberculosis is the most important. The importance of droplet inhalation is demonstrated by the fact that over 90% of tuberculosis fatalities are caused by pulmonary tuberculosis.

Mycobacterium tuberculosis is the most common cause of human tuberculosis and, with very few exceptions, is the result of direct person-to-person spread. The proportion of cases caused by *M. bovis* is significant in developing countries, where animal tuberculosis is widely distributed, there is close contact between animals and their owners (e.g. penned overnight in close proximity), control measures are not consistently applied and pasteurisation is rarely practiced. In industrialised countries the proportion of cases caused by *M. bovis* is much lower, as a result of animal tuberculosis control and elimination programmes, together with milk pasteurisation (Cosivi *et al.*, 1998).

Infected people may not develop symptoms as their immune system can usually control the bacterium, sometimes throughout life. However inactive bacteria can become active again later in life, particularly if the immune system is weakened. Reactivation of *M. bovis* infections acquired prior to widespread milk pasteurisation is a significant contributor to the current incidence of infection with this organism (Cousins and Dawson, 1999).

This Risk Profile is concerned with risks of primary intestinal infection, and the symptoms below principally concern this form of the disease.

Supplemental information on adverse health effects is given in Appendix 2.

4.1 Symptoms

Incubation: Tuberculosis is characteristically a slowly developing chronic condition. In airborne infections and in immunocompetent people the incubation period can be years, while in immunosuppressed people it may be months. Cases of the gastrointestinal form can occur after reactivation of primary infections occurring many years earlier.

Symptoms: Fever, chills, weight loss, abdominal pain, diarrhoea or constipation. Other symptoms depend on the organs infected. Symptoms may last for months or years.

Condition: Intestinal tuberculosis or tuberculous enteritis. Human tuberculosis due to *M. bovis* is indistinguishable clinically from tuberculosis due to *M. tuberculosis*.

People Affected: Immunosuppressed people are especially at risk of either acute infection or reactivation of an infection acquired in the past. In countries where infection is uncontrolled, children are at greater risk of infection.

Treatment: Multiple antibiotic treatment is required to be administered over protracted periods (Collins, 2000). This is because the organism may have antibiotic resistance and this will not be apparent for long periods because of the slow growth of the organism.

Vaccination: The vaccine used in humans against tuberculosis is the Bacillus Calmette-Guérin (BCG) made from live, weakened *M. bovis*. The vaccine was introduced around 80 years ago and is the most widely used vaccine in the world. However, its efficacy is highly variable, ranging from 0 – 80% (ACET, 1996).

4.2 *Mycobacterium bovis* and AIDS

Patients with AIDS are susceptible to opportunistic infections, and outbreaks of multi-drug resistant tuberculosis have been reported amongst such patients. While *M. tuberculosis* is the most common agent identified, outbreaks within hospitals involving *M. bovis* have also been reported (Bouvet *et al.*, 1993; Samper *et al.*, 1997; Gori *et al.*, 1998). These hospital outbreaks have not been linked with foodborne transmission. Several studies have found an association between human *M. bovis* disease and HIV co-infection, although, in one of these outbreaks, the index case had possibly acquired the infection in Brazil where the prevalence of *M. bovis* in cattle is reported up to 18% (Bouvet *et al.*, 1993).

4.3 Dose Response

No specific human dose response studies for ingestion of *M. bovis* were located. Results from animal experiments (on sheep, cattle and guinea pigs) in the early 20th century indicate that infection via the oral route requires thousands or millions more organisms than infection via the inhalation route. Research on guinea-pigs demonstrated that 1 to 62 bacilli caused pulmonary infection whereas it took 10mg of tubercle bacilli by the oral route (16-18 million times more) (Sigurdsson, 1945).

A bovine model of infection developed for vaccine and diagnostic studies (Hewinson *et al.*, 2003) showed that for the respiratory route (intratracheal) challenge with 10^3 - 10^4 colony forming units of *M. bovis* generated symptoms as seen in the natural disease, whereas challenge with higher doses (10^5 - 10^6 cfu) produced atypical lesions.

4.4 Incidence

Tuberculosis is a notifiable disease in New Zealand. The incidence of reported tuberculosis in New Zealand has been stable for the last ten years, at approximately 10 per 100,000 population (350-450 cases per annum).

An analysis of the incidence of human tuberculosis caused by *M. bovis* using data from Wellington Hospital from 1983 to 1990 found that an average of 7.2% of cases of tuberculosis were caused by this organism (Brett and Humble, 1991). The most common organ affected was the lung (pulmonary tuberculosis) which suggests that the disease was not caused by contaminated meat or milk. Instead it was suggested that the primary source may be exposure to domestic or wild animals. The risks are higher in those areas where there is a wildlife reservoir of *M. bovis*, especially the possum.

Approximately 50 – 75% of the cases of tuberculosis are able to be confirmed by the identification of an isolated organism; for the remaining cases the causative *Mycobacterium* species is unknown. *M. tuberculosis* is distinguished from *M. bovis* on the basis of biochemical tests and antibiotic and drug susceptibility. Information on the relative

proportions of *M. tuberculosis* to *M. bovis* isolates obtained from recent cases in New Zealand is given in Table 3.

Table 3: Identity of *Mycobacterium* isolates from tuberculosis notifications and laboratory sources in New Zealand, 1997 - 2007

Year	Number of isolates identified			Reference
	Total	<i>Mycobacterium tuberculosis</i>	<i>Mycobacterium bovis</i> (percentage of total)	
1997	330	194	6 (3.0%)	ESR, 1998
1998	368	248	8 (3.1%)	Perks <i>et al.</i> , 1999
1999	456	297	5 (1.7%)	Kieft <i>et al.</i> , 2000
2000	353	242	8 (3.2%)	Lopez <i>et al.</i> , 2001
2001	381	283	6 (2.1%)	Sneyd <i>et al.</i> , 2002
2002	384	264	4 (1.5%)	Sneyd and Baker, 2003
2003	418	316	6 (1.9 %)	ESR, 2004
2004	372	283	5 (1.7%)	ESR, 2005a
2005	348	257	5 (1.9%)	ESR, 2006*
2006	358	258	8 (3.0%)	ESR, 2007*
2007	290	222	3 (1.3%)	ESR, 2008*

*These figures are referenced in the main surveillance reports, but actual data on isolates were included in the anti-microbial resistance report (www.surv.esr.cri.nz/antimicrobial/tuberculosis.php).

The percentage of tuberculosis cases from which *M. bovis* was identified appears to have decreased in New Zealand from an average of 7.2% in 1983-1990 (Brett and Humble, 1991) to approximately 3% in 1996-2001, decreasing to below 2% between 2002 and 2007 (except for the year 2006). Based on the proportion of *M. bovis* isolates amongst those identified, and the total reported cases of tuberculosis, the incidence of *M. bovis* infection in recent years (2005-2007) is approximately 0.1-0.3 per 100,000 per year.

The details of the approximately 70 notified cases of infection with *M. bovis* from 1995 to 2007 were reviewed for this document. For three cases, one each in 1998, 1999 and 2002, a food was noted among the risk factors recorded; in all three cases this was unpasteurised milk. In none of these cases was the infection conclusively linked to the milk, and one case was a dairy farm worker who could have acquired the infection via exposure to animals. This is supported by the fact that the site of the infection was pulmonary. One other case (an older adult) reported consuming unpasteurised milk as a child. There were no cases for which meat consumption was reported as a risk factor.

Of 11 notified *M. bovis* cases between 2006-2007, two mentioned food as a factor in their histories. In the first case, a New Zealand born 67 year old male contracted a new infection of *M. bovis*, the site of the infection was pulmonary and he was hospitalised. The case had consumed unpasteurised bovine milk in his childhood (1939 – 1955) and also drank unpasteurised bovine milk as a farm worker from 1955 – 1965.

In the second case of a 41 year old male, the infection was new, with the site of the infection being pulmonary. The case had worked at a milk factory in the late 1980s, and a dairy farm in the early 1990s making cheese and packing milk and yoghurt. However, unpasteurised milk consumption was not recorded. A second “other confirmed” case involved a close

family member who was 11 months old, again the infection was recorded as pulmonary. Person-to-person transmission was thought to be the route of infection; however, no culture or genetic typing was performed. As an epidemiological link only, it cannot be confirmed that this was an outbreak with person-to-person transmission.

Fifty percent of notified *M. bovis* infections were reported as having pulmonary infections, a further 6% had both pulmonary and extrapulmonary infections, while the site of infection was unknown in 15% of cases. There was no consistent pattern in the site of extrapulmonary infections, although four instances of infection of the cervical lymph node were reported. Infection at this site was more common prior to milk pasteurisation (Grange, 1995) and, given the age of the cases (55-80), these cases may represent reactivation of old infections.

Risk factors reported for *M. bovis* infections included; farm or meatworks contact (9% of cases), other animal contact (research, veterinary clinic; 4%), occupational exposure (lab technician; 2%), overseas travel or residence (Pacific Islands, South Africa, Iraq; 15%).

A combined epidemiological and laboratory investigation of cases of *M. bovis* infection in New Zealand from 1998 to 2002 (Baker *et al.*, 2003) reviewed 38 cases in detail. Compared with people infected with *M. tuberculosis*, people infected with *M. bovis* were significantly more likely to be male, over 60 years of age, European or Maori, to have been born in New Zealand rather than being immigrants, and to be living in the South Island at the time of diagnosis. *M. bovis* infection was no more associated with extra-pulmonary sites of infection than *M. tuberculosis*.

Typable isolates were obtained for 18 of the 34 cases; 11 of these were similar types to those previously seen in New Zealand wild or domestic animals. No animal reservoir appeared to dominate. Four cases reported animal contact that could potentially have given rise to infection. Although its small size precluded establishing modes of infection, the study did conclude that *M. bovis* infection in New Zealand was not increasing, despite the large reservoir of infection in this country.

4.5 Clinical Outcomes Tuberculosis in New Zealand

Hospitalisation and fatality rates for notified cases of tuberculosis (from both *M. tuberculosis* and *M. bovis* infection) in New Zealand are given in Table 4. These outcomes are not always reported for each case, so percentages are expressed in terms of the number of cases for which outcomes are known.

Table 4: Outcome data for tuberculosis in New Zealand. 1997 - 2007

Year	Hospitalised cases	Fatalities	Reference
1997	229/293 (78.2%)	15/330 (4.5%)	ESR, 1998
1998	251/340 (73.8%)	8/368 (2.2%)	Perks <i>et al.</i> , 1999
1999	273/408 (66.9%)	14/456 (3.1%)	Kieft <i>et al.</i> , 2000
2000	199/314 (63.4%)	8/353 (2.3%)	Lopez <i>et al.</i> , 2001
2001	213/334 (63.8%)	2/381 (0.5%)	Sneyd <i>et al.</i> , 2002
2002	193/348 (55.5%)	6/384 (1.6%)	Sneyd & Baker, 2003
2003	206/361 (57.1%)	5/358 (1.4%)*	ESR, 2004
2004	203/322 (63.0%)	5/323 (1.5%)*	ESR, 2005b
2005	175/302 (57.9%)	4/348 (1.1%)	ESR, 2006
2006	172/325 (52.9%)	5/358 (1.4%)	ESR, 2007
2007	142/257 (55.3%)	3/290 (1.0%)	ESR, 2008

*For these years, the number of cases for which death data were recorded was reported and this has been used as the dominator. For other years, this figure was not reported and the total number of tuberculosis cases has been used as the denominator.

A summary of overseas information on *M. bovis* infections is presented in Appendix 2. These data indicate that proportion of total tuberculosis cases estimated to be caused by *M. bovis* in New Zealand (1-3%) is similar to other developed countries

5 EVALUATION OF RISK

5.1 Estimate of Risk for New Zealand

5.1.1 Risks associated with milk

If it is assumed that approximately 3% of all notified cases of tuberculosis in New Zealand are caused by infection with *M. bovis*, then the current incidence of tuberculosis caused by this organism is approximately 0.3 per 100,000. However, there is no conclusive evidence that these infections are caused by transmission from milk. Given that pulmonary infections are at least as prevalent as extra-pulmonary infections, acquisition of infection by inhalation rather than ingestion of food appears to be important, possibly via occupational contact with infected animals.

Unpasteurised milk used to be a common vehicle for transmission of *M. bovis*. However, since the introduction of mandatory pasteurisation, milk has largely ceased to be a vehicle. Since 1995, two cases of *M. bovis* infection (out of approximately 70) in New Zealand have reported consuming unpasteurised milk among the risk factors recorded, but in neither case was this vehicle confirmed.

Pasteurisation is sufficient to control *M. bovis* in milk. There is likely to be some consumption of unpasteurised milk on New Zealand farms, and from sales of milk at a few farm gates. A recent study of transmission of *Campylobacter* in a semi-rural community found that consumption of unpasteurised milk was not uncommon, with 20% of respondents reporting consumption of unpasteurised milk (Baker *et al.*, 2002). However, as a proportion of total national milk consumption this amount will be very low.

Part of the Animal Health Board's control measures include testing of the majority of New Zealand dairy cattle, and these tests show a very low prevalence of bovine tuberculosis. This means that the risk of consuming *M. bovis* contaminated unpasteurised milk will be similarly low.

5.1.2 Risks associated with other foods

No evidence has been found that would implicate foods other than milk (and raw milk cheese) in the transmission of *M. bovis*. A Risk Profile on *M. bovis* in red meat (Cressey *et al.*, 2006b) did not find any evidence of transmission via meat.

5.2 Risk Categorisation

The proportion of severe outcomes (hospitalisation, long term sequelae, and death) resulting from *M. bovis* infection in New Zealand should be considered as high. The course of the disease has a long term (months or years) duration and a mortality rate of 3.1% has been reported for tuberculosis in New Zealand.

In 2007 the population rate (including reactivations) of tuberculosis in New Zealand, based on notifications, was 6.9/100,000. Testing of isolates from 2005-2007 identified *M. bovis* in 1-3% of tuberculosis cases, giving a *M. bovis*-related tuberculosis rate of 0.1-0.3/100,000 of population.

Out of 11 notified *M. bovis* cases between 2006-2007, two reported unpasteurized milk consumption, with the linkage not being confirmed in either case. If this linkage was assumed to be valid this would equate to a milk-related population rate of *M. bovis* infection of approximately 0.05/100,000.

There is little evidence for foodborne transmission of *M. bovis* to humans in countries where milk pasteurisation is mandatory or widely used. This is also the case for New Zealand. The effective protection afforded by pasteurisation is backed up by an infection control programme in cattle.

Based on this information, the risk from this hazard/food combination will be infinitesimal when milk is pasteurised. Any risk of human infection in New Zealand would derive from the consumption of unpasteurised milk or dairy products that came from infected dairy cattle. The prevalence of consumption of these products is difficult to estimate, but the disease control measures in place (57% of dairy cattle in New Zealand were tested in 2006-2007) would reduce this risk to a very low level.

6 AVAILABILITY OF CONTROL MEASURES

Given the mandatory pasteurisation of almost all milk in New Zealand, the potential exposure of New Zealanders to *M. bovis* in this food is minimal. There appears to be little reason to conduct a quantitative risk assessment.

6.1 Limitations and caveats

Although information to estimate the prevalence of raw milk consumption is limited, data on risk management of *M. bovis* infection in cattle are extensive, giving confidence in this assessment of low risk.

The data gaps identified in this Risk Profile are:

- Prevalence (if any) of *M. bovis* in the raw milk of infected animals detected by Animal Health Board testing;
- Tuberculosis status of milking goats in New Zealand, and production of goats milk for consumption; and,
- Dose response relationship for *M. bovis* infection in humans via the gastrointestinal route.

6.2 Current risk management measures

Risk management measures for *M. bovis* in milk are targeted at two levels, control of the organism in the food, and control of the pathogen in animal reservoirs

6.2.1 Relevant food controls

The New Zealand (Milk and Milk Products Processing) Standard 2007 contains a number of risk management options for unpasteurised milk and associated products. The primary risk management measure for raw milk in New Zealand is the requirement that the milk is harvested under an approved Risk Management Programme (RMP) appropriate for milk that is intended for direct human consumption. To date no RMP has been approved for the harvesting of raw milk intended to be sold in this manner.

In terms of unpasteurised milk products, these are either cheeses that are made from thermised milk and undergo a “cheese treatment”, or raw milk cheeses that are manufactured under the methods set down by the Swiss Federal Council (dated 18th October 1995) for Emmental, Gruyere or Sbrinz. To date no RMP or FSP has been approved for the manufacture of an unpasteurised cheese in New Zealand using cheese treatment or the Swiss cheese methods.

6.2.1.1 *Raw milk*

The sale of raw milk is restricted to farm gate sales and in effect, no raw milk can be sold or resold in New Zealand except to end users in small quantities, or to milk processors. This exemption was originally in the Milk Act 1988 (repealed 1990) and is now in Section 11A of the Food Act 1981. The amount of milk sold at the farm gate is limited to 5 litres or less at any one time.

The Food Act 1981 (reprint 3 September 2007), Section 11A states the following;

“Restriction on selling raw milk.

(1) Except as provided in subsections (2) and (3) of this section, no person shall sell, resell or buy any raw milk.

(2) A milk producer may sell raw milk to any person if –

a) It is sold –

i) at the producer’s dairy premises; and

ii) in a quantity not exceeding five litres at any one time; and

b) The person intends the milk for consumption by the person or the person’s family;- and the person may buy it accordingly”.

(3) A milk producer may sell raw milk to a dairy processor (as defined in section 4 (1) of the Animal Products Act 1999) who –

a) purchases the milk for processing for sale or export; and

b) is a person who –

i) carries out the processing under a risk management programme registered (or deemed to be registered) under the Animal Products Act 1999 or under a food safety programme (as defined in section 4 (1) of that Act) or

ii) carries out processing of a kind that is exempt under section 9 of that Act from the requirement for a risk management programme; or

(iii) is a person or business who, by section 79 of the Animal Products (Ancillary and Transitional Provisions) Act 1999, is at the time of the sale excused from the requirement to operate under a registered risk management programme or a food safety programme.

(4) This section is subject to section 9.

6.2.1.2 Pasteurised milk

The introduction of pasteurisation is credited with virtually eliminating human foodborne exposure to *M. bovis*. Consequently it is relevant to consider the situation regarding pasteurisation of milk in New Zealand.

The Food (Milk and Milk Products Processing) Standard 2007 is the basis for determining heat treatment or alternative standards for milk or milk products. In terms of pasteurised milk, the treatment must be in accordance with once of the following;

(1) “holding method” (63°C to 66°C for at least 30 minutes),

(2) “high temperature short time” method (72°C for at least 15 seconds), or

(3) any other heat treatment method that is as effective in terms of bacterial reduction as methods (1) and (2).

The most commonly used pasteurisation method for milk products is the “high temperature, short time” method. Extended shelf life and ultra heat treated products are pasteurised at 120-124°C and 134-135°C (or higher) respectively, for short periods. The “holding method” is occasionally used for batch pasteurisation for certain products. The efficacy of pasteurisation is always checked by phosphatase enzyme based assays (Chris Erikson, Mainland Products, personal communication).

Currently the food legislation in New Zealand and Australia is progressing towards a single code for both countries. At present the joint Food Standards Code exists in parallel with local Australian and New Zealand legislation. The Food Standards Code Standard 2.5.1 stipulates that milk in Australia must be processed according to Standard 1.6.2 of the Code. This describes pasteurisation in terms of time and temperature (72°C for no less than 15 seconds), although alternative times and temperatures may be used provided the same lethal effect on bacteria is achieved.

6.2.2 Control of bovine tuberculosis in New Zealand

M. bovis, the causative agent of bovine tuberculosis, is a notifiable organism under the Biosecurity (National Bovine Tuberculosis Pest Management Strategy) Order 1998 (Livingstone, 2002).

A national bovine tuberculosis pest management strategy (NPMS) for both cattle and deer operates under the Biosecurity Act and is administered by the Animal Health Board (O’Neil and Pharo, 1995; Livingstone, 1996). An important component of this programme is the consideration of wild animal vectors of tuberculosis, especially possums. A voluntary eradication scheme for deer was introduced in 1985 and this became compulsory in 1990.

The Animal Health Board NPMS has a primary objective of reducing New Zealand’s Tb period prevalence to fewer than 0.2% infected herds by 2013 (AHB, 2007). Progress objectives towards this include:

- To prevent the establishment of vector populations (principally ferrets and possums) infected with Tb in areas that are Tb-vector free from 1 July 2004. Since June 2004, there have been no confirmations of newly established vector populations in vector free areas,
- To increase the area deemed to be Tb-free to at least 226,000 km² (84%) of New Zealand’s land area by 30 June 2006. An area of 223,000 km² was declared Tb-free by this timeframe,
- To reduce the mean annual number of infected vector-related breakdowns in herds located in Tb-vector risk areas to no more than 12 breakdowns to every 1000 uninfected herds (AHB, 2005).

The control of bovine tuberculosis infection in New Zealand is measured by the number of infected herds. Measures are the **period** prevalence of infected herds (the number of infected herds at the beginning of the previous 12 month period plus any additional herds identified during the period as a percentage of the total herds) or **point** prevalence (the number of infected herds within an area of interest at a particular time as a percentage of the total herds within the area). Recent data on period and point prevalence of tuberculosis in animals in New Zealand come from the Surveillance publication website:

<http://www.biosecurity.govt.nz/publications/surveillance/index.htm> and are summarised in Table 5. These data indicate the continuation of a downward trend in prevalence seen in both cattle and deer herds since 1992/1993.

Table 5: Point and period prevalence for tuberculosis in cattle and deer herds in 2001 to 2007

Year	Point prevalence*		Period prevalence*	
	Cattle herds	Deer herds	Cattle herds	Deer herds
2001	414 (0.62%)	92 (1.67%)	1.23%	2.51%
2002	364 (0.5%)	79 (1.5%)	0.99%	2.35%
2003	275 (0.4%)	67 (1.3%)	0.82%	2.19%
2004	235 (0.3%)	73 (1.4%)	0.69%	1.84%
2005	185 (0.26%)#	50 (0.96)#	0.57%§	1.71%§
2006	153 (0.22%)Δ	31 (0.64%)Δ	0.45%Δ	1.27%Δ
2007	130 (0.18%)Δ	18 (0.38%)Δ	0.39%Δ	

* As at 30 June of the relevant year

From Animal Health Board annual report (<http://www.ahb.org.nz/NR/rdonlyres/79CB90CA-EBCE-46F7-BEB0-153E42860FB6/263/Section5AHBAR2005.pdf>)

§ From Terry Ryan, NZFSA.

Δ From AHB, Annual Report (2007)

A country or area is considered to be free of tuberculosis when 99.8% of the herds in the area have been officially free for 3 years. New Zealand is approaching this level. At the end of June 2007, the period prevalence was 0.39% (AHB, 2007). Given the extensive tuberculosis control programme for both cattle and deer, intensive meat inspection procedures which ensure that infected meat is not exported, and the mandatory pasteurisation of milk in New Zealand (apart from very small quantities sold directly from farms), it has been considered that this issue would not cause any trade problems (O'Neil and Pharo, 1995).

The control programme involves both repeated testing of live animals (with slaughter of infected stock) and examination of all carcasses in licensed slaughter premises for lesions (Montgomery, 1999). Controls are in place for the movement of stock between uninfected areas, and regions where infection is endemic (Ryan and Livingstone, 2000). At year ending June 2007, notified diagnoses of tuberculosis in animals were as follows: cattle (130), deer (18) (AHB, Annual Report 2007). Ninety-two percent of infected cattle herds were located in Vector Risk Areas, overall 77% were in the South Island and 42 % were dairy herds (AHB, Annual Report, 2007).

An important component of the control programme is the control of wild animal vectors of tuberculosis, especially brush-tailed possums. Tuberculous possums and occasionally other feral animals such as ferrets have been identified in 18 discrete areas of New Zealand in association with persistent infection in cattle and deer herds. These Vector Risk Areas cover approximately 34% of New Zealand's land area. The remainder is classified as Vector Free. It is estimated that 90% of new infections in cattle and deer herds are caused by possums and ferrets (AHB, Annual Report 2007).

6.2.3 Economic costs of risk management

The extreme rarity of cases of infection with *Mycobacterium bovis* caused by foodborne transmission means that the cost to New Zealand in public health terms will be negligible.

The cost of tuberculosis disease control in animals is substantial with the strategy funded by the Crown and industry (under voluntary agreements and by way of regulatory levies). The Animal Health Board Annual Report states that \$78.6 million for the 2007 year was spent,

\$52 million on vector control and \$17 million on disease control (primarily 4.9 million cattle tests).

A cost-benefit analysis of *M. bovis* eradication in the United States showed that costs were outweighed by reduced numbers of cattle lost (and therefore lower replacement costs), as well as reduced losses of milk and meat production (Nelson, 1999).

6.3 Options for risk management

The New Zealand Food Safety Authority is currently considering a proposed framework for the manufacture, importation and sale of raw milk products in New Zealand (Discussion Document 04/08). This is concurrent with similar considerations by Food Standards Australia New Zealand for Australia (Proposal P1007).

In this context, it is relevant to consider the potential risk from *M. bovis* in milk, should the requirement for mandatory pasteurisation be removed. It is assumed that Animal Health Board controls on bovine tuberculosis would be maintained at their current level. In this scenario the risk from *M. bovis* in raw milk is considered to remain low due to the low prevalence in cattle as demonstrated by the Animal Health Board testing, and the indications that the dose-response relationship for ingestion is markedly lower than for the respiratory route. However, due to the potential for mixing of milk during distribution, consideration could be given to instituting additional controls on raw milk and raw milk products from positive dairy herds, and in areas where *M. bovis* infection in wildlife reservoirs is endemic.

6.4 Summary

The combination of an effective tuberculosis pest management strategy with mandatory pasteurisation of almost all milk in New Zealand means that the risk from *M. bovis* in milk will be very low. The absence of notified cases of tuberculosis where transmission via milk has been confirmed supports this conclusion.

Further risk management measures to control this risk appear to be unnecessary.

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APPENDIX 1: HAZARD AND FOOD

The information contained in this Risk Profile is current to the date of publication. Please be aware that new information on the subject may have arisen since the document was finalised.

The following information is taken from a number of different sources but, unless otherwise referenced, is primarily derived from a data sheet prepared by ESR under a contract for the Ministry of Health in 2000-2001. The data sheets are located on the NZFSA website and are intended for use by regional public health units. The datasheets will be updated from time to time, and placed on this website:

<http://www.nzfsa.govt.nz/science/data-sheets/index.htm>

1.1 *Mycobacterium bovis*

1.1.1 Growth and survival

Growth:

Characteristics of the "tuberculosis complex" that distinguish them from other *Mycobacteria* include slow growth, with growth reported at 37°C, but not 25°C or 45°C (Jenkins *et al.*, 1992). A minimum growth temperature of approximately 30°C is reported for *M. tuberculosis* (Spahr and Url, 1994). Given the short shelf life of foods that it has been associated with, e.g. unpasteurised milk and raw meat, growth in foods is unlikely to be significant. The organism requires oxygen to grow but grows optimally in environments that contain less oxygen than atmospheric levels (i.e. ~20%).

Survival:

Temperature: Survival is better under cool conditions. *M. bovis* survived in cow faeces for five months in winter but only two months in summer (O'Reilly and Daborn, 1995). A New Zealand study employing *M. bovis* absorbed on cotton ribbons demonstrated that survival times on pasture, the forest floor or in brushtail possum dens were shorter in summer, and longer in spring and winter (Jackson *et al.*, 1995).

Water Activity: Survives dry conditions well.

1.1.2 Inactivation (CCPs and Hurdles)

Temperature: Inactivated by normal pasteurisation. Further details given in section 3.2.

Radiation: Inactivated by sunlight.

1.2 The Food Supply in New Zealand: Milk

Milk is intended to meet the demands of the suckling newborn through nourishment and to provide immunological protection. Whole cow's milk is made up of water (approximately 87.3%), fat (4.2%), lactose (4.6%), protein (3.2%) and minerals (0.6%). These proportions vary according to breed of animal, feed, age, and phase of lactation (ICMSF, 1998).

Since milk has an almost neutral pH (6.7), a high water content and a variety of nutrients, it represents an ideal substrate for microbial growth. This is countered to some extent by natural inhibitory factors in raw milk. The main inhibitory factors in raw milk are the lactoperoxidase system (which produces hypothiocyanate which inactivates enzymes and damages membranes) and lactoferrin (which binds iron) (Frank, 2007). Guidelines have been issued by Codex (1991) on the preservation of raw milk by activating the lactoperoxidase system, although this method should only be used when technical, economical or practical reasons do not allow the use of cooling facilities and where the product is not being exported from the country of origin.

To the year ended 31 May 2006, three co-operatively owned dairy companies produced the following percentages of total milk solids; Fonterra Co-operative Group Ltd (95.3%), Westland Co-operative Dairy Company Limited (3.2%) and Tatua Co-operative Dairy Company Limited (1%). Twelve other companies process the remaining 0.5% (MAF, 2007).

Fonterra is a leading multinational dairy company and is the world's largest dairy products exporter, exporting 95% of its production. The company is owned by 10,921 dairy farmers, who are shareholders, and employs 16,400 people. The company collected 14.34 billion litres of milk to year end May 2007 (Fonterra website, accessed 3rd April 2008; <http://www.fonterra.com>).

APPENDIX 2: EVALUATION OF ADVERSE HEALTH EFFECTS

Tuberculosis is the general name for a group of diseases associated with the presence of *Mycobacterium* spp. (MTBC), of which pulmonary (lung) tuberculosis is the most important. Although infection usually affects the lungs it can affect almost any organ, usually spreading via the lymphatic vessels. Various manifestations of the disease are known as scrofula and consumption. The organism is less commonly found in muscle tissue, or in parts of the body with few blood vessels.

Ingested *M. bovis* is protected from digestion by the waxy coating of the bacterium. The ileocecal region (junction of small and large intestines) is the main site of infection for ingested organisms, where the bacterium migrates to mucosal glands and establishes an inflammatory process. Bacteria are carried to Peyer's patches (part of the lymphatic system) by phagocytes which results in the formation of tubercles (a site of infection characterised by a granular appearance) which can later necrose and release organisms causing further (secondary) sites of infection (Vanderpool and O'Leary, 1988).

Intestinal tuberculosis can occur either through direct ingestion of the organism (primary tuberculous enteritis) or due to the spread of the disease after pulmonary infection (secondary).

This Risk Profile is concerned with risks of primary intestinal infection, and the symptoms below principally concern this form of the disease. However, it should be noted that oral exposure to *M. bovis* can also cause cervical lymphadenopathy, a tumour-like inflammation of the lymph nodes in the neck also known as scrofula (Grzybowski and Allen, 1995). In some cases the affected nodes may rupture through the skin, resulting in sinus formation and occasionally chronic skin tuberculosis (lupus vulgaris; Grange, 2001). The combination of lymphadenopathy and lupus vulgaris is termed scrofuloderma.

2.1 Typing

Stable genotypes of *M. bovis* have been identified and various typing methods have been used in the field, especially when investigating the epidemiology of new outbreaks in animals. Van Embden *et al.* (1995) have reviewed typing methods. These include Restriction Fragment Length Polymorphism (RFLP) or Restriction Enzyme Analysis (REA) of genomic DNA and techniques that use a range of polymorphic genetic markers, including two insertion sequences IS6110 and IS1081, and three small repetitive DNA elements: the major polymorphic tandem repeat (MPTR), the direct repeat (DR) and the polymorphic GC rich repeat (PGRS). Kremer *et al.* (1999) has described further typing techniques based on a repeat GTG sequence and analysis of exact tandem repeat (ETR) loci using Variable Number of Tandem Repeats (VNTR) typing. Kamerbeek *et al.* (1997) developed a technique known as spacer oligonucleotide typing (spoligotyping) for typing of *M. tuberculosis* isolates, that has subsequently been applied to *M. bovis* (Cousins *et al.*, 1998).

In New Zealand the REA of *M. bovis* has been developed and is now used routinely. Over a period of 23 years, approximately 2,700 isolates of *M. bovis* from domestic animals and wildlife have been examined and classified into over 250 different DNA types. (Ryan *et al.*, 2006).

DNA fingerprinting of *M. tuberculosis* isolates has been useful in understanding the epidemiology of human transmission. The original typing method for *M. tuberculosis* is not useful for *M. bovis* due to the absence of the relevant genetic sequence in the *M. bovis* genome. However, the newer method (MIRU-VNTR) (Kremer *et al.*, 1997), based on a different genetic sequence, is allowing studies of the epidemiology of both organisms. These are usually studies of animal epidemiology, but it has also been applied to human cases (Evans *et al.*, 2007). This method is currently employed in New Zealand by AgResearch.

2.2 Adverse health effects overseas

A review of the incidence of human tuberculosis caused by *M. bovis* in industrialised countries showed that the proportion of total tuberculosis cases attributable to *M. bovis* was approximately 7% or less, with a high proportion (31 – 73%) being pulmonary tuberculosis (Cosivi *et al.*, 1998). This suggests predominantly airborne transmission unrelated to food.

In Europe, the European Food Safety Authority has collated information on tuberculosis due to *M. bovis*. In 2005, 17 member states and one non-member state reported data, among these, 9 member states reported 119 cases, see Table 5 (EFSA, 2007). This is a 25.3% increase on the 2004 figure of 95 reported cases. Cases from Germany and the UK account for 77.3% of the notifications. EFSA have also broken down the cases into age groups, in 2005, 60 of the 119 cases were recorded as being above 65 years old. Wide variability in reporting means that further data interpretation is not meaningful. For comparison, New Zealand also has a recent rate of 0.1-0.3 per 100,000.

Table 6: Number of confirmed *M. bovis* cases, rate per 100,000 and country TB status in European countries

Country	Confirmed cases	Rate 100,000 population	Country's TB status*
Austria	6	<0.1	OTF
Czech Republic	2	<0.1	OTF
Germany	53	<0.1	OTF
Ireland	3	<0.1	Not OTF
Italy	7	<0.1	Not OTF ⁺
Malta	1	0.3	Not OTF
Spain	4	<0.1	Not OTF
Sweden	4	<0.1	OTF
United Kingdom	39	NR	Not OTF
Total	119		

NR: No report

* OTF = Officially tuberculosis free

+ 11 provinces are OTF (Officially Tuberculosis Free).

Thoen *et al.*, (2006) have produced a table of case reports, reviews and epidemiological reports concerning human tuberculosis cases due to *M. bovis* between the decades of 1966 – 2005 and by region or country (reproduced in Table 6). Overall the data suggest a decline for the decade 1976-1985 but rising to the previous decades' numbers post 1986. However, these data do not take into account, progress in medical diagnoses and also population changes over the time surveyed.

Table 7: Case reports, reviews and epidemiological reports concerning human tuberculosis cases due to *M. bovis* (1966-2005), by decade and country

Regions/countries	1966-1975	1976-1985	1986-1995	1995-2005
Western Europe	37	10	31	36
Eastern Europe	13	9	4	0
United States/ Canada	7	7	16	10
Latin America	3	1	5	3
Australia/ New Zealand	0	1	6	2
Africa	5	1	2	11
India, Israel, Taiwan, Turkey	0	0	3	3
WHO/ OIE, FAO, IUATLD	2	0	3	3
Total	67	29	70	68

Grange (1995) has summarised data from Germany, United Kingdom, Denmark, France, Poland, Hungary, Switzerland, Czechoslovakia and Turkey prior to 1965. *M. bovis* infection accounted for 1.1 (Poland) to 10.5% (Germany) of total tuberculosis cases and there was a higher proportion of non-pulmonary cases (12.1-90.0%) than pulmonary (0.2-5.9%) cases.

Kleeberg (1984) reviewed data from a wider range of countries, mainly from dates prior to 1960. Several general observations can be made from the reviewed information presented:

- *M. bovis* infection represented a higher proportion of total tuberculosis cases in children than in adults.
- *M. bovis* infections represented a higher proportion of non-pulmonary cases than pulmonary.
- The contribution of *M. bovis* infection to total tuberculosis cases appears to have decreased during the latter half of last century.

In France an incidence of 0.07/100,000 cases of tuberculosis caused by *M. bovis* has been recorded (Boulaïbal *et al.*, 1999). *M. bovis* was the causative agent in only 0.5% (38 of 7075) of tuberculosis cases examined. Of the 38 cases, three could be attributed to the consumption of unpasteurised milk.

In England and Wales 1.2% (117 of 9687) of tuberculosis cases examined by the PHLS Communicable Disease Surveillance Centre between 1986 and 1991 were caused by *M. bovis*. When supplementary data were included, information for 228 cases was available. Of these, 122 (53%) were from patients aged over 60 years and were attributed to the reactivation of infection acquired prior to the institution of control measures. Around 22% of the particular body sites infected suggested that the organism could have been ingested (Hardie and Watson, 1992). Cases were attributed to either 1) reactivation of old infections or 2) cases brought into the UK by immigrants.

Between 1993 and 1999 annual reported case numbers of tuberculosis caused by infection with *M. bovis* in the UK ranged between 30 and 50. Around 75% of patients were aged 50 years or over, suggesting reactivation of infections acquired earlier. As there has been an increasing incidence of herd “breakdown” (presumably infection) in cattle, enhanced surveillance of *M. bovis* in humans was instituted in 1998 with the aim of investigating risk factors for transmission of the bacterium to humans (PHLS, 2001). However, case numbers

in the UK have continued to decrease and in the period 2000-2003 were in the range 17 to 34 (de la Rua-Domenech, 2006). This represents less than 0.5% of all new tuberculosis notifications.

A stable incidence of 0.56 cases/100,000 has been reported for Ireland over the period 1983-1992 (Cotter *et al.*, 1996). Fifty-three percent of *M. bovis* cases involved pulmonary infection. No rural-urban difference could be detected in rates and it was concluded that the initial infection was likely to have occurred in childhood through the consumption of unpasteurised milk.

Cousins and Dawson (1999) reviewed the information available on *M. bovis* infections in Australia from 1970 to 1994. The mean number of cases per year was 9.4, representing approximately 1% of Australian cases of tuberculosis during this period. Data were available for 150 patients. A high proportion (71.6%) of patients suffered pulmonary disease. Only one case suffered from infection at the gastrointestinal site, two in the meninges and five in the lymph nodes; sites typical for gastrointestinal infection. Males were more than twice as likely to be infected by the organism, perhaps reflecting occupational exposure. It was considered that most cases of extra-intestinal infection result from reactivation of chronic infections, some of which would have been acquired by the consumption of milk before pasteurisation became commonplace. Many of the patients in the study had a history of working in the livestock industry, including abattoirs.

A study in Australia on isolates obtained between 1970 and 1994, using IS6110, PGRS, DR and spoligotyping, showed that most Australian-born patients working in the livestock industry had infection with organisms similar to those isolated from cattle, suggesting occupational exposure. Patients born outside of Australia yielded different types indicating that they had been exposed to the organism prior to entry into Australia (Cousins *et al.*, 1999).

A study of Swedish isolates, using RFLP and probing for IS6110, showed a distinct type among cases in farmed deer, which was distinct from types involved with cases of disease in humans, camels and cats. The degree of precision was not detailed enough to determine the clonal status of the human isolates (Szewzyk *et al.*, 1995).

Van Soolingen *et al.* (1994) used IS6110, DR and PGRS typing to demonstrate that most human cases of *M. bovis* infection in Argentina were due to transmission from cattle, while human infections in the Netherlands were mainly contracted from animals other than cattle.

2.1.1 Contributions to outbreaks and incidents

No information on this could be located. This may be because foodborne incidents of bovine tuberculosis are very rare, or that such data are not kept. Given the severity of the disease, the former of these explanations is the most likely.

2.1.2 Case control studies

Besser *et al.* (2001) conducted a case-control study to examine potential source of *M. bovis* tuberculosis infection in children in San Diego, CA, USA. Cases were more likely to have received Bacillus Calmette-Guérin (BCG) vaccine against tuberculosis (OR = 44), been born

overseas (OR = 4.3) and to have consumed raw milk or cheese (OR = 3.76) and the high prevalence of bovine tuberculosis in Mexican cattle was discussed. A multi-agency investigation in New York city identified 35 cases of human *M. bovis* infection between 2001 and 2004. The anatomical site of disease was extrapulmonary in 21 (60%) patients, pulmonary in 9 (26%) patients and both in 5 (14%) patients. Almost all of the cases were adults born outside the USA (predominantly Mexico) or children of Mexican-born parents. Soft fresh unpasteurized cheese imported from Mexico was identified as the likely source of infection (Winters *et al.*, 2005).

A similar recently reported outbreak of *M. bovis* in the USA has been traced to illegal unpasteurized dairy products including 'queso fresco' (ProMED, 2008). The outbreak among Hispanic immigrants in Southern California is thought to have originated from cattle in Mexico where *M. bovis* infects approximately 17% of the herds. *M. bovis* accounts for around 10% of all new tuberculosis cases in the California/Mexico border region.

2.1.3 Risk assessments and other activity overseas

Humans re-infecting cattle and acting as reservoir hosts is theoretically possible but little scientific literature could be found on the subject. A documented case of human to cattle transmission of bovine-type tubercle bacteria was published in the Netherlands (Tesink, 1970, reported in Thoen *et al.*, 2006).

Australia

A key difference between Australia and New Zealand in terms of tuberculosis status is that the native brushtail possum has not become naturally infected with *M. bovis* in Australia. This has been attributed to the low population density of possums in the Australian bush, as opposed to the high population densities encountered in New Zealand. (In addition, possums have a lack of predators in New Zealand). In relation to other reservoir hosts in Australia, the feral pig is considered an end host. Feral water buffalo and cattle were formerly reservoir hosts until they were destroyed during an eradication campaign. The water buffalo population in Australia is now totally derived from a tuberculosis-free population (Radunz, 2006).

Australia was declared Tuberculosis Provisionally Free in 1992 and Impending Free status in 1997. The last detection of tuberculosis in cattle was in 2000, in Queensland. The last detection in a feral host was in two water buffalo in 2002, located in the Northern Territories.

Through the eradication of *M. bovis* from Australia's cattle and water buffalo herds, the risk of exposure has declined significantly, but human cases of *M. bovis* infection are likely to continue to be detected for years to come due to reactivation of old lesions.

United Kingdom

During the compilation of a report on the health risks from consuming meat from cattle with *M. bovis* infection (ACMSF, 2001), the Committee was not asked for its views on the risk from drinking raw milk. However guidance in this matter was clarified. The Dairy Products (Hygiene) Regulations 1995 require raw cows' milk to come from animals belonging to a herd that has been declared officially tuberculosis free (OTF), otherwise the milk must be

heat treated. Where the State Veterinary Service becomes aware of a TB reactor, or suspicious lesions at routine slaughter in a dairy herd are found, the OTF status is suspended and a statutory heat treatment notice is served by the local Food Authority. The Committee therefore considered those who consumed pasteurised cows' milk to be well protected by the legislation and control measures in place.

Ireland

The Food Safety Authority of Ireland published a report in July 2003 (Food Safety Authority of Ireland, 2003) which considered the potential for transmission of zoonotic tuberculosis through the food chain, particularly via milk and meat. In Ireland, there is a requirement that cow's milk intended for sale must be pasteurized, with exceptions for milk processed into certain types of cheese. Herds that supply registered raw cheese producers must have two tuberculin herd tests annually (there are 25 such herds supplying to 20 processors in 2003). No milk may be used from reactor animals although milk from non-reactor animals in the same herd can be used if heat-treated. Raw milk products must also be labeled as such. There are no legal requirements for the pasteurisation of goat's milk and no routine tuberculin test if the holding has no cattle. However, where goats are kept on holdings with cattle, the herd must have an annual test.

The two principal sources of concern for the potential transfer of *M. bovis* via milk are consumption of unpasteurized cow's or goat's milk and consumption of raw milk cheeses, both described in more detail under the European assessment below. The available evidence in Ireland however suggests that the level of *M. bovis* in raw milk cheese is likely to be very low and overall zoonotic tuberculosis is rare. Transmission through milk from infected cattle herds has been a major public health issue in the past, but pasteurisation has largely eliminated the problem.

Europe

The Scientific Panel on Biological Hazards have expressed an opinion on the risks to human health due to tuberculosis in bovine animals (European Scientific Panel on Biological Hazards, 2003). Although the majority of the document addresses the risk associated with the consumption of meat, there is a chapter devoted to milk. The small number of cases in Europe is attributed principally to immigrants from less developed countries, or reactivation of a latent infection. In developing countries, zoonotic tuberculosis associated with consumption of raw milk and dairy products produced from infected cattle and goat herds has been compared to the disease in Great Britain in the 1930s. Where approximately 40% of animals slaughtered at public abattoirs had tuberculosis lesions and about 0.5% of all dairy cows produced milk containing tubercle bacilli (Thoen *et al.*, 2006).

The European Scientific Panel identified two principal sources of concern regarding the potential transfer of *M. bovis* to consumers via milk;

- Consumption of raw cows' milk amongst farming families and their visitors, and
- Production of cheeses made from unpasteurised milk and intended for consumption in the raw state. The impact of the cheese production process on the viability of *M. bovis* is not well defined and the cheese production process has not been demonstrated to eliminate viable *M. bovis*. In addition, validated methods for the

detection of *M. bovis* in milk or milk products are not routinely available. A period of 6 weeks may have elapsed between point of infection and time to development of positive reactor status which means that infection may have occurred any time in the 6 weeks immediately prior to or since a negative tuberculin test (Food Safety Authority of Ireland, 2003).

The effect of salt, pH and heat on a related micro-organism, *M. avium* var. *paratuberculosis* during production of a soft white Hispanic-style cheese was studied (Sung and Collins, 2000). Salt had little or no effect on inactivation while lower pH values were significantly correlated with decreasing D values. The authors concluded that heat treatment of raw milk coupled with a 60-day curing period will inactivate about 10^3 cells per ml.

2.1.4 Secondary transmission

Person-to-person spread may occur, most probably by the inhalation route. However, the likelihood of this occurring is not great with Grange (2001) describing it as an “exceptional event”.

Most reports of human-to-human transmission are largely anecdotal, although van Soolingen *et al.* (1994) identified the same strain in three members of one family and another person in the same apartment building. None of the cases had frequent contact with domesticated or other animals. A more recent report in the Lancet (Evans *et al.*, 2007) identified two epidemiologically-linked cases of human *M. bovis* infection in the Midlands, UK. This led to all patients infected by *M. bovis* between 2001-2005 ($n=20$) to have their isolates assessed by DNA fingerprinting. A cluster of patients infected by the same strain was identified and cases interviewed. All six cases were young and UK-born. Five had pulmonary disease and one died due to *M. bovis* meningitis. Five had received BCG vaccines as children, including the fatal case. All patients had common social links through visits to bars in two different areas. With the exception of the first case, there was an absence of zoonotic links or consumption of unpasteurized dairy products. The authors concluded that a series of person-to-person transmissions had occurred. The first case had a history of occupational contact with cattle and had consumed unpasteurised milk and cheese.

Co-infection with *M. bovis* and HIV increases the likelihood of tuberculosis development and a nosocomial outbreak amongst HIV patients has been reported (Bouvet *et al.*, 1993).