UK Publicly Funded Research Relating to *Mycobacterium avium* subsp. *paratuberculosis*

Report from the Microbiological Safety of Food Funders Group

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UK Publicly Funded Research Relating to *Mycobacterium avium* subsp. *paratuberculosis*
Research from 1990 to 2005

OVERVIEW

This report is the output of a review by the Microbiological Safety of Food Funders Group (MSFFG) of the research relating to *Mycobacterium avium* subsp. *paratuberculosis* (MAP) supported by its member organisations from 1990 to the end of 2005. Although not a major research area for any member organisations of the MSFFG, there has been significant research addressing the reduction and elimination of MAP in milk. This has been based on the precautionary principle of seeking to reduce human exposure to MAP and does not consider whether there is a link between MAP and Crohn's disease.

MAP is the causative organism of Johne's disease (paratuberculosis) in a variety of animals, primarily domestic ruminants. It has been suggested that it is associated with Crohn's disease in humans. The current consensus opinion is that there is insufficient evidence to either prove or disprove a causal link between MAP and Crohn's disease. Since the primary source of infection with MAP is an infected animal, research focuses on the possibility of zoonotic transfer of MAP to humans through the food supply chain.

Research during the period of the report has focused primarily on the effect of heat treatment on MAP and elimination of the organism from milk. There has been only limited further research on other aspects, reflecting the uncertain status of the organism in relation to food-borne disease and also the practical difficulties in working with the organism.

Although not the focus of research addressed in this report and supported by the MSFFG member organisations, results of relevance to the understanding of the relationship between MAP and Crohn's disease do not suggest that the current view should be modified.
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LAY OVERVIEW

Mycobacterium avium subspecies *paratuberculosis* (MAP) causes Johne's disease (paratuberculosis), a prolonged and often fatal disease in cattle and other farm animals. Some of the clinical signs of the disease in cattle are similar to those of Crohn's disease in humans, and it has been suggested that MAP may contribute to the human illness. As yet, there is no definitive evidence to prove or disprove the suggestion that this may be the case, and MAP is therefore not regarded as a food-borne pathogen.

On the principle of seeking to reduce a possible, if unconfirmed, risk, research has been supported in recent years to find ways of removing or destroying MAP in milk, so as to reduce exposure of humans to the pathogen. Some research is also in hand to investigate specific aspects of the bacterium which may lead to a clearer understanding of any possible relationship between it and disease in humans. None of the research has given evidence to conclusively disprove or support the idea that MAP may be involved in Crohn's disease.

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1. INTRODUCTION

1.1 The Microbiological Safety of Food Funders Group (MSFFG) has previously published reports giving an overview of the research funded by member organisations of the MSFFG relating to various food-borne pathogens including Verocytotoxin-producing *Escherichia coli*[1], *Campylobacter*[2], *Salmonella*[3], *Listeria monocytogenes*[4], *Yersinia enterolitica*[5] and food-borne viruses[6]. As part of the ongoing process of considering research into all food-borne pathogens supported by MSFFG members, the group has undertaken a review of research on *Mycobacterium avium* subsp. *paratuberculosis* (MAP), as recorded in this report.

1.2 This report gives an overview of the progress of research relating to MAP and the possibility for its transfer to humans through the food supply chain undertaken in the UK and funded by members of the MSFFG. It summarises research in the period from 1990 to the end of 2005 and seeks to set this in the context of other research and issues within the UK and overseas. In addition, an assessment is made of those areas where further research might be needed.

1.3 MAP is the causative agent of Johne's disease, or paratuberculosis, in animals. Paratuberculosis is a highly infectious, chronic and generally fatal disease. It occurs throughout the world and is considered by the Office International des Epizooties as a disease of major global importance[7]. It occurs most commonly in domestic ruminants such as cattle, sheep and goats, but also in wild animals including red deer and rabbits (Grant (2005)). Infection of the animal usually occurs shortly after birth, and animals are most susceptible to infection during the first year of life. Signs of disease are rarely apparent until two or more years after initial infection, and include weight loss and diarrhoea (accompanied by normal appetite) generally leading to further deterioration and death. Animals infected with MAP when beyond their first year of life are not likely to develop the clinical disease until they are older than two years.

1.4 MAP is a member of the family Mycobacteriaceae, which includes *Mycobacterium tuberculosis,* the causative agent of tuberculosis in humans.

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[1] http://www.food.gov.uk/science/research/researchinfo/foodborneillness/microfunders/vtec

[2] http://www.food.gov.uk/science/research/researchinfo/foodborneillness/microfunders/campylobacter

[3] http://www.food.gov.uk/science/research/researchinfo/foodborneillness/microfunders/msffg/55669

[4] http://www.food.gov.uk/science/research/researchinfo/foodborneillness/microfunders/listeria

[5] http://www.food.gov.uk/science/research/researchinfo/foodborneillness/microfunders/yersinia

[6] http://www.food.gov.uk/science/research/researchinfo/foodborneillness/microfunders/msffg/msffgfbv2005

[7] http://www.oie.int/eng/maladies/en_classification.htm#ListeOIE where the disease is called paratuberculosis

In the environment, MAP is unable to multiply outside of its susceptible animal hosts but it can survive for long periods in soil and water before infection of a new susceptible host through, for example, consumption of contaminated material. Thus the primary route of infection is from an infected animal, either directly or indirectly.

1.5 In 1913 it was suggested that Crohn's disease in humans, which has some of the same clinical symptoms as those of paratuberculosis, might also be associated with infection by MAP. The view now is that several different factors contribute to Crohn's disease, including genetic predisposition and environmental factors as well as an abnormal inflammatory response. The current consensus is that there is insufficient evidence to either prove or disprove a link between MAP and Crohn's disease in humans, but that the hypothesis is still plausible (Rubery (2002), Grant (2005)). As a consequence, there is a degree of interest internationally in the possible transmission of MAP to humans, including through the food chain. The possible routes of transmission of MAP to humans through the food chain could potentially include milk and milk products, beef and drinking water (Grant (2005)). Given that heat treatment is often used as a means of killing bacteria in food, a complication is that there is evidence that MAP can survive pasteurisation temperatures (Chiodini and Herman-Taylor (1993), Grant *et* al (1996)) although possibly only when present in high numbers (Grant *et al* (1998)). In recognition of the specific possibility of humans being exposed to MAP through milk, coupled with the issue of the recorded heat resistance of MAP, the FSA is developing a strategy for the control of MAP in cow's milk[8]. This is based on the precautionary principle of seeking to reduce human exposure to MAP and does not rely upon establishing a link between MAP and Crohn's disease.

2. METHODS

2.1 This report is based on those research projects that are funded by the member organisations of the MSFFG. At the time of writing this report, these were the Food Standards Agency (FSA), the Department for Environment, Food and Rural Affairs (Defra), the Biotechnology and Biological Sciences Research Council (BBSRC), the Department of Health (DH), the Department of Agriculture and Rural Development, Northern Ireland (DARD), the Environment Agency, the Food Safety Promotion Board (FSPB), FSA Scotland, FSA Wales, FSA Northern Ireland, the Health Protection Agency (HPA), the Meat and Livestock Commission (MLC), the Medical Research Council (MRC), the Scottish Executive Environment and Rural Affairs Department Science and Research Group (SEERAD SRG) and the Scottish Executive Department of Health (SEDH).

2.2 The MSFFG project database[9] was used to identify projects for inclusion in this report. The MAP-related projects were identified by searching the

[8] http://www.food.gov.uk/multimedia/pdfs/map_strategy.pdf

[9] The MSFFG maintains a database containing information about research projects in the area of the microbiological safety of food that are funded by the members of the MSFFG. Members of the Group provide the project information from their respective project record

database for the terms “MAP”, “Mycobacteria” and “paratuberculosis”. The projects identified by this approach were checked and a number removed from consideration as they focused on genomic mapping and were not related to MAP at all. In addition, members of the MSFFG were requested to identify any projects which might have been omitted from the MSFFG project database. This gave a total of 30 projects which are listed in Appendix 2. The earliest of these projects was initiated in 1990.

2.3 Studentships were omitted from consideration.

2.4 Research funded by other agencies, including the Wellcome Trust, Royal Society and NHS Scotland as well as international research is not included within the body of the report. However, a summary of research funded through these bodies is given in section 3 below.

3. RESEARCH SUPPORTED BY OTHER FUNDING BODIES

3.1 The international research community for paratuberculosis is relatively small[10]. At the 8th International Colloquium on Paratuberculosis[11] held in 2005, the principal areas of research which were discussed were the prevention and control of paratuberculosis at both national and domestic ruminant herd level, the molecular biology of the pathogen, in particular genomics and comparative genomics, the pathogenicity of MAP in the context of the animal disease, the diagnosis and epidemiology of MAP in ruminants and wild animals and the implications of the presence of MAP in certain contexts for public health. The last research area is of particular relevance to this report. Research from around the world addressed common themes of the possible transmission of MAP to humans through water supplies, the survival and removal of MAP from milk and the presence of MAP in healthy individuals and those with Inflammatory Bowel Disease (IBD), of which Crohn’s disease is a form.

3.2 An important contribution to the study of MAP and other mycobacteria is the publication of the genome sequences of several members of the genus including *M. tuberculosis* (Cole *et al* (1998)), *Mycobacterium leprae* (Cole *et al* (2001)), *Mycobacterium bovis* (Garnier *et al* (2003)) and recently MAP itself (Li *et al* (2005)). These enable extensive species comparisons and offer the possibility to develop an understanding of the differences in the genetics and molecular biology of the organisms, and why their host ranges, and pathogenicity, vary so extensively. The whole genome sequence has also allowed recognition of new target sequences that can be used to develop primers for polymerase chain reaction (PCR) assays that may be of value in detection of the organism (Stabel and Bannantine (2005)).

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systems. The earliest projects within the database were initiated in 1990. Some historic project data from member organisations joining the MSFFG in 2005 (eg the EA, HPA, MLC, MRC) may be unavailable to the database. www.msffg.org.uk

[10] See http://www.paratuberculosis.org/index.htm for information

[11] http://www.paratuberculosis.org/index.htm

4. RESEARCH SUPPORTED BY THE MEMBER ORGANISATIONS OF THE MSFFG

4.1 Isolation and detection of MAP

4.1.1 The isolation and detection of MAP is hampered by the difficulties in culturing the organism in the laboratory, and the very slow growth rates it shows both in the laboratory and in susceptible animals. In addition, the organism does not grow and multiply in the environment, but can persist in soil and water for significant periods of time. There are also a number of other strains of *Mycobacterium avium* subsp. *avium* which occur in the environment and which are associated neither with paratuberculosis nor Crohn's disease. If an understanding of the possible exposure of humans to MAP is to be achieved, it will be necessary to develop methods for detecting the organism in relevant environments, including milk and milk products, and for differentiating it from other *M. avium* subspecies.

4.1.2 Techniques for the isolation of MAP from milk and water used either filtration (**FSPB 00-RESR-046**), centrifugation (**FSA FS1210),** a combination of both (**Defra WT02013**), or immunomagnetic separation (**MAFF FS1042**) as methods to concentrate the organisms. Chemical protocols for selectively recovering MAP from milk and cheese have also been investigated (**FSA B01003**). All the methods developed were demonstrated as being able to isolate predicted levels of MAP from the chosen environments.

4.1.3 Several projects focussed on the development of techniques for detecting MAP in milk and milk products (**FSA FS1210**, **FSPB 00-RESR-046, 00-RESR-060, MAFF FS1256**). Techniques investigated included the use of monoclonal antibodies (**FSPB 00-RESR-060**) and PCR (**FSA FS1210**, **FSPB 00-RESR-060, MAFF FS1256**). The exploitation of molecular biology techniques is of particular relevance, and two projects have included research on insertion sequences as a method for differentiating between MAP and other subspecies of *M. avium* that occur in the environment (**FSA FS1210**, **SEERAD MRI07101**). The latter project has also led to the identification of MAP specific proteins which are up-regulated *in vivo* and are therefore regarded as putative virulence factors of interest as potential targets for drug intervention, or in vaccine development (**SEERAD MRI07101**).

4.2 Occurrence and epidemiology

4.2.1 MAP is endemic throughout most of the world. There has been no specific monitoring of its occurrence within the UK. Relevant information may come from a survey of MAP infection in cattle funded by Defra which is due to start during 2006 and which includes determining the prevalence of MAP in dairy cattle herds. Epidemiological research supported by the MSFFG member organisations focuses on the potential interaction between MAP in different susceptible animal groups and, ultimately, humans.

4.2.2 The role of wildlife, including rabbits, in the epidemiology of farmed ruminants in Scotland has been investigated (**SEERAD MRI82797, BSS82797, SAC82797** and **SAC31601**). The overall results suggest that MAP occurs in a wide range of wild animals, including deer, rabbits and predators such as foxes and stoats. Rabbits were a particular focus of research and it was found that MAP could be recovered from around 40% of rabbits examined. It was also noted that cattle and sheep ingested rabbit faecal pellets when they grazed, providing a risk of exposure of the animals to MAP in contaminated pellets (**SEERAD SAC31601**). Data were obtained showing that isolates of MAP from rabbits were capable of infecting calves leading to pathology consistent with early Johne's disease (**SEERAD MRI82797, BSS82797** and **SAC82797**).

4.2.3 The occurrence of MAP in cattle in both Ireland and Scotland has been the subject of research projects (**FSPB 00-RESR001**, **SEERAD SAC31701**). The presumption is that a principal route of transmission of MAP to humans is through milk and other dairy products. To explore this, the incidence of MAP in raw cows', sheep and goats' milk in England, Wales and the Republic of Ireland has been investigated (**FSA B08001**, **FSPB 00-RESR-046**). The incidence of MAP in sheep and goats' milk was negligible, with no MAP being isolated from sheep milk and the organism being found in one out of 90 samples of goats' milk. It was concluded that these are unlikely to be a significant route for the transmission of the organism to humans. In contrast, MAP was detected in milk filters in a study in Ireland (**FSPB 00-RESR-046**) and in over 10% of milk samples tested in a wider study of both raw and pasteurised cows' milk (**FSA B08001**). In the latter study viable MAP could be isolated from a small proportion (1.6-1.8%) of both raw and pasteurised milk samples and it was concluded that cows' milk, even after pasteurisation, could be a possible vehicle for transmission of the organism to humans. In a separate study examining the effectiveness of analyses of raw milk for microbial contamination, MAP was detected in 4% of raw milk samples (**FSA B12002**).

4.2.4 Using an assay for insertion sequences unique to MAP in order to determine whether MAP was present in pasteurised milk for sale in England, it was found that overall 7% of the 312 samples from cartons and bottles tested positive for MAP (**FSA FS1210)**. MAP could eventually be cultured from half of these milk samples.

4.2.5 The possibility that MAP could persist into the manufacturing process of cheese has been investigated (**DARD 0030 41913**). It was found that in a laboratory model process for cheddar cheese production spiked with MAP, the organism persisted through at least the full six months of cheese ripening allowed in the process. In laboratory experiments, viable MAP could be recovered for up to 35 days from soft cheese made with MAP-spiked raw milk and stored at 4°, although the levels of MAP declin ed with time. MAP was also detected in a variety of unpasteurised cheeses purchased from a supermarket, but viable MAP could not be isolated (**FSA B01003**).

4.2.6 Studies of the occurrence of *Mycobacterium* spp in different water supply systems found that they were present in up to 60% of the samples analysed, but only in low numbers. Mycobacteria occurred more frequently in lowland river water than groundwater. The situation was less clear with upland reservoir water (**Defra WT02013, WT02033**). MAP itself was not isolated from any of the 187 samples analysed (**Defra WT02033**). It was not clear whether the absence of MAP was a genuine result or a reflection of the difficulties in isolating and identifying the organism. However, it was noted that there is widespread public exposure to mycobacteria in general, including *M. avium* subsp. *avium*.

4.2.7 As discussed above (section 1.5), it is possible but unproven that MAP is implicated in Crohn's disease. The hypothesis that exposure to water, milk or dairy products potentially contaminated with MAP would be associated with an increased occurrence of Crohn's disease was examined (**Defra WT02028**). It was concluded that the study did not provide any evidence of an increased risk in Crohn's Disease associated with exposure to MAP in water or milk. In addition, there was no association between farm holidays or contact with farm animals and Crohn's Disease. The same study observed an association between meat consumption and the risk of developing Crohn's disease. As such a link was not one of the hypotheses being tested in the research programme, the result is difficult to interpret and requires further investigation.

4.3 Pathogenicity and molecular biology

4.3.1 Research into the pathogenicity and molecular biology of MAP is limited, in part because of the difficulties of working with the organism in the laboratory. Research projects have been funded to identify virulence genes in MAP (**BBSRC S06531**) with a view to developing mutants as the basis for vaccines, and to explore molecular approaches to understanding the pathogenicity of MAP again with a view to prophylaxis (**SEERAD MRI04598, MRI06801** and more recently **SEERAD MRI08804**). Techniques necessary for gene knock-out experiments have been established including a paratuberculosis infection model in mice (**SEERAD MRI04598**). An understanding of the regulation of identified possible virulence genes in MAP has been developed using some of these techniques. The mouse model has been used to assess the virulence of MAP isolates from different host species, which will be important in developing an understanding of the epidemiology of the organism (**SEERAD MRI06801**). Further work in this area is being undertaken (**SEERAD MRI08804**).

4.3.2 Developing an understanding of the pathogenicity of MAP in ruminants is limited by the absence of models for the disease. Two such models, addressing the course of the disease from initial infection through to adult life, have been developed and are being used in research to understand paratuberculosis (**SEERAD MRI03096**). The gene expression patterns of ovine macrophages from MAP-infected animals are being assessed in order to understand the host response to MAP infection (**SEERAD MRI05800**). As part of this project, oligonucleotide arrays for appropriate ruminant genes

(immuno-inflammatory genes) are being constructed.

4.4 Reduction and elimination

4.4.1 A number of projects have focussed on the early finding that, at least under laboratory conditions, MAP is able to survive standard pasteurisation (**MAFF FS1042**, **FS10363**, **FSA B08001**). Further research demonstrated that higher pasteurisation temperatures did reduce the numbers of viable MAP in milk but it was still possible to demonstrate the presence of low levels of viable MAP after such treatments (**FSA B01003**). Extended holding times at the standard pasteurisation temperature were found to be more effective at inactivating MAP and it was concluded that this approach was more likely to achieve complete inactivation of MAP than increased temperature.

4.4.2 There has been some debate about the validity of laboratory pasteurisation experiments, and work has been done to demonstrate that MAP can be found in commercially pasteurised cows' milk (**FSA B08001**). Other research demonstrated that MAP could be isolated from milk spiked with the pathogen and then treated with high temperature for a short time, whereas *M. bovis* could not be recovered after such treatment (**MAFF FS1038**). The growing evidence is that a proportion of any population of MAP exhibits heat resistance which, whatever its cause, presents a possible route for MAP to be introduced into the human food supply chain. Research has been undertaken to determine methods for making a significant reduction in MAP levels in pasteurised milk using approaches which can be used by the dairy industry (**Defra FQS14**). Homogenisation prior to pasteurisation, centrifugation and microfiltration were found to offer possible methods capable of achieving this level of reduction.

4.4.3 Pasteurisation of milk and other elimination methods will be more effective if the initial load of bacteria in the raw milk is as low as practicable. Hazard analysis has identified that the cleanliness of the teats of dairy cows immediately prior to milking is important and research has been undertaken to identify optimal cleaning regimes that will be most effective at removing bacteria, thereby reducing the levels of bacteria including MAP present in raw milk (**FSA B12003**).

4.4.4 In one project (**SEERAD SAC31701**) it was noted that some farmers and veterinarians did not regard paratuberculosis as being as important clinically or economically as other cattle diseases. This could have implications for management of the illness.

5. GAPS IN CURRENTLY FUNDED RESEARCH

5.1 A significant issue with respect to MAP for the MSFFG is the question of whether the organism is zoonotic, although issues of animal health as affected by MAP and impacting on the food-supply chain are also important. There are a number of gaps in research with MAP and MAP-associated illness, filling of which could improve understanding of the zoonotic potential of the bacterium

as well as its significance for animal health.

5.2 There is a need for the development of improved cheap, sensitive and specific isolation, diagnostic and quantification tests for the bacterium. These would be valuable in epidemiological studies including in wildlife as well as in farm animals and other environments such as foods. Where testing of foods is concerned, assays also need to be able to distinguish between viable and non-viable MAP.

5.3 With farm animals in particular, there are significant gaps in understanding of the pathogenicity of MAP and its interaction with host animals, as well as in the epidemiology of MAP, including the effect that cattle herd size would have on MAP infections.

5.4 The role of protozoa as 'Trojan horses' acting as vehicles of transmission for MAP to animals and also enabling it to survive for prolonged periods in the environment is unclear and may need to be determined.

5.5 Although there have been extensive studies of the survival of MAP in liquids (eg milk) there is no equivalent research with solid food (eg beef) as the food matrix. This area may also require further consideration.

5.6 It is probable that there will be research supported in areas not directly relevant to the microbiological safety of food which will be relevant to the zoonotic potential of MAP. The international interest in the pathogenicity of mycobacteria in general is likely to lead to a greater understanding of the pathogenicity of MAP as genomic studies are undertaken. Worldwide research into Johne's disease is likely to provide insights into aspects of the epidemiology of MAP and its possible transmission to humans.

6. CONCLUSIONS

6.1 Research supported by the member organisations of the MSFFG addresses many different areas of relevance to the microbiological safety of food. Much of the research supported in relation to MAP is precautionary, based around survival and detection of MAP in foods. Unless it is established that MAP is a food-borne pathogen, it is unlikely that there will be significant change in the research direction or effort on MAP in the context of food-borne diseases.

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APPENDIX 1: GLOSSARY

Crohn's disease
A chronic inflammatory disease of the human digestive tract, especially involving the small intestine and large intestine.

Johne's disease (also known as paratuberculosis)
Johne's disease is a contagious, chronic and usually fatal infection that affects primarily the small intestine of ruminant animals. All ruminants are susceptible to Johne's disease. The disease is caused by *Mycobacterium paratuberculosis,* a hardy species of bacterium related to the agents of leprosy and tuberculosis. The disease is worldwide in distribution. For more information see http://www.aphis.usda.gov/vs/nahps/johnes/ and http://vetgate.ac.uk/browse/cabi/0747da35bcf252d51de6cff0307b0ba1.html

Zoonosis/Zoonotic
Diseases and infections which are transmitted naturally between vertebrate animals and man.

APPENDIX 2: MSFFG PROJECTS USED IN THIS REPORT

Project Code	Title	Funder	Contractors	Start Date	End Date
S06531	Identification of virulence genes in *Mycobacterium paratuberculosis* by allelic exchange	BBSRC	University of Surrey	Sep-1996	Oct-2000
0030 41913	Investigation of the incidence and persistence of *Mycobacterium avium* subsp. *paratuberculosis* (map) in food and its possible role in Crohn's disease	DARD	Queens University Belfast	Aug-2000	Aug-2003
FQS14	Reduction of risk associated with contamination of raw milk by *Mycobacterium avium* spp. *paratuberculosis*	Defra	Queens University Belfast, Hannah Research Institute	Jan-2001	Feb-2004
WT02013	Fate of *Mycobacterium avium* complex in drinking water treatment and distribution systems	Defra	Health Protection Agency (HPA)	Oct-2001	Dec-2002
WT02028	A study of sources of drinking water and Crohn's Disease	Defra	University of East Anglia	Dec-2002	Dec-2004
WT02033	Further studies on the incidence of *Mycobacterium avium* Complex and *Helicobacter* organisms in water supplies	Defra	Health Protection Agency (HPA)	Oct-2001	Sept-2003
B01003	Characterisation of the non-linear thermal inactivation kinetics observed with *Mycobacterium paratuberculosis* in milk	FSA	Queens University Belfast	Apr-1997	Aug-2000
B08001	Survey of the incidence of *Mycobacterium paratuberculosis* (MAP) in cows', sheep and goats' milk in England, Wales and N. Ireland	FSA	Queens University Belfast	Apr-1997	Oct-2000
B12002	Review of raw milk analyses methods and assessment of effectiveness as pathogen markers and indicators of farm hygiene	FSA	Direct Laboratory Services	Jul-2002	Jun-2004
B12003	Investigation of the effectiveness of pre-milking teat cleaning regimes	FSA	University of Wolverhampton and Harper Adams University College	Oct-2002	Sep-2004
FS1210	Testing food for *Mycobacterium paratuberculosis* and pathogenic atypical *Mycobacteria* using highly specific DNA probes	FSA	St. Georges Hospital	Dec-1990	Dec-1993

Project Code	Title	Funder	Contractors	Start Date	End Date
00-RESR001	Epidemiological assessment of *Mycobacterium avium* subsp. *paratuberculosis* (MAP) in target Munster herds	FSPB - Food Safety Promotion Board (NI)	Queens University Belfast	May-2003	Oct-2004
00-RESR046	Detection and molecular characterisation of selected pathogenic organisms isolated in unpasteurised milk using milk filters.	FSPB - Food Safety Promotion Board (NI)	Queens University Belfast, Cork County Council	Jan-2001	Sep-2004
00-RESR060	Development of rapid tests for the detection of *Mycobacterium avium* subsp. *paratuberculosis* (MAP) and their use to determine survival in food matrices	FSPB - Food Safety Promotion Board (NI)	Queens University Belfast, National University of Ireland	Feb-2001	Jan-2004
FS1036	Investigation of the thermal death of *Mycobacterium paratuberculosis* at pasteurisation temperatures	MAFF	Queens University Belfast	Sep-1994	Aug-1995
FS1038	Survival during high temperature short time pasteurisation by *Mycobacterium paratuberculosis*	MAFF	Veterinary Laboratories Agency	Apr-1994	Mar-1995
FS1042	Thermal inactivation of low levels of *Mycobacterium paratuberculosis* in milk by HTST pasteurisation	MAFF	Queens University Belfast	Sep-1993	Oct-1996
FS1256	Investigations of PCR methods for MAP in milk	MAFF	LGC	Nov-1996	Apr-1997
BSS82797	Role of wildlife in the epidemiology of paratuberculosis of farmed ruminants. (FF)	SEERAD	Biomathematics & Statistics Scotland (BIOSS)	Apr-1998	Jun-2002
MRI03096	Immunobiochemical studies on host-pathogen interactions in ovine paratuberculosis	SEERAD	Moredun Research Institute	Apr-1996	
MRI04598	Molecular approaches to investigate the pathogenesis of, and prophylaxis for, *Mycobacterium avium* subspecies *paratuberculosis*.	SEERAD	Moredun Research Institute	Apr-1998	Mar-2001
MRI05800	Comparative expression profiling in the three defined forms of ovine paratuberculosis. (FF)	SEERAD	Moredun Research Institute	Nov-2000	Mar-2005

Project Code	Title	Funder	Contractors	Start Date	End Date
MRI06801	Molecular approaches to investigate the pathogenesis of, and prophylaxis for, *Mycobacterium avium* subspecies *paratuberculosis*	SEERAD	Moredun Research Institute	Apr-2001	Mar-2004
MRI07101	Identification and analysis of difference between IS901+ *Mycobacterium avium* and *Mycobacterium avium* subspecies *paratuberculosis*. (FF)	SEERAD	Moredun Research Institute	Feb-2002	Mar-2006
MRI08804	Pathogenesis Of *Mycobacterium avium* subspecies *paratuberculosis* Infections.	SEERAD	Moredun Research Institute	Apr-2004	Mar-2006
MRI82797	Role of wildlife in the epidemiology of paratuberculosis of farmed ruminants. (FF)	SEERAD	Moredun Research Institute	Jan-1998	Dec-2000
SAC31601	Role of rabbits and the environment in the epidemiology of paratuberculosis of farmed ruminants. (FF)	SEERAD	Scottish Agricultural College	Oct-2001	Mar-2005
SAC31701	Occurrence management and perception of risk associated with paratuberculosis in cattle.	SEERAD	Scottish Agricultural College	Oct-2001	Jun-2004
SAC82797	Role of wildlife in the epidemiology of paratuberculosis of farmed ruminants. (FF)	SEERAD	Scottish Agricultural College	Apr-1998	Jul-2001