Johne’s Disease

Questions and Answers

1. What is Johne's Disease?
Johne's Disease is an infectious wasting condition of cattle and other ruminants caused by *Mycobacterium avium* subspecies *paratuberculosis* (often known as *Map*). It is a chronic gastrointestinal infection of adult ruminants. The disease progressively damages the intestines of affected animals. The disease is characterised by profuse and persistent diarrhoea, severe weight loss, emaciation, loss of condition and infertility. Affected animals eventually and inevitably die. In dairy herds, the presence of Johne's Disease will significantly reduce milk yields well before other signs of the disease can be found. Although not a notifiable disease in Great Britain, Johne's Disease is notifiable in Northern Ireland. It has a worldwide distribution.

Map

2. What is *Mycobacterium avium* sub-species *paratuberculosis* (*Map*)?
Mycobacterium avium sub-species *paratuberculosis* is a bacterium pathogenic to animals that is primarily found in the digestive tract of wild and domestic herbivorous (grass eating) animals throughout the world. It has been known for many years to be the cause of Johne's Disease in cattle, sheep, goats and other ruminants and some camelids, e.g., alpacas. It also causes disease in other animals, e.g., rabbits, pigs and horses.

3. Is *Mycobacterium avium* subspecies *paratuberculosis* (*Map*) the same as *M. paratuberculosis* (MPTB)?
Yes, it is also called *M. paratuberculosis* or *Map* for short.

4. Can bacteria causing Johne's Disease live in the environment and, if so, for how long?
The *Map* bacterium is tough and can live for months and even more than a year under the right conditions. It does die off in the environment and the main factors that reduce its viability are sunlight and heat. Its survival is probably also affected by chemicals and competition with other microbes. Further research is being undertaken now to determine if enough bacteria are surviving in the environment for prolonged periods to actually infect animals.

5. How is *Map* spread?
Diseased animals in general pass large numbers of *Map* in their faeces (dung). A single diseased animal can therefore pose a high risk to susceptible animals and in particular to the young calves in the herd. Diseased animals may also excrete *Map* in milk and colostrum. While cattle remain susceptible to infection throughout life, they are at their most vulnerable in the first few months of life. Calves may be infected in the womb but are more commonly infected through:

- drinking contaminated colostrum;
- ingesting dung that may be present on unclean teats;
- contaminated feed; and
- contaminated water supplies.

Further information about how *Map* is spread may be found at Appendix 1.

6. When are animals most likely to become infected?
Under field conditions it is considered that the disease is normally transmitted to animals at an early age, usually under 30 days old, principally by the ingestion of feed or water contaminated by faeces from infected animals. It is believed that some calves may be infected in the womb before they are born, and the bacteria can also be present in the milk of infected cows.

Johne's

7. Why should farmers care about Johne's Disease?
The disease can have a significant financial impact on farmers through loss of output, poor health and early culling. Animals that are visibly sick with Johne's Disease are uncommon in most infected herds. However, such obvious illness can build up if the infection is not controlled in the herd.

The impact on a business can be severe if Johne's Disease is introduced into a beef herd, particularly for herds selling breeding animals or retaining home-bred replacements. Minimising the risk by sourcing cattle from herds that can demonstrate a low risk of being infected is the most effective precaution that producers can take when introducing animals. A negative herd test is one component of assuring low risk.

It has been suggested that *Map* may also be a possible cause of Crohn's Disease in humans. Such a causal link between the two conditions has yet to be proved or disproved, however the Government is taking a precautionary approach in this area. A possible route to infection in humans could be through consumption of milk containing *Map*.

Control and prevention of Johne's Disease makes sound long term sense for three reasons:
1. to reduce or prevent loss of production and income that results from this disease;
2. to increase the value of your breeding stock if your herd is certified as free of the disease
3. to reduce the level of *Map* in milk and the environment.

The Food Standards Agency has published a strategy for reducing the levels of *Map* in milk. The strategy includes the following components:

- hygienic milking practices;
- effective pasteurisation of milk;
- reducing the level of *Map* in dairy herds.

For more information visit www.food.gov.uk/safereating/microbiology/mapinmilk/ and for more information on dairy hygiene refer to www.defra.gov.uk/corporate/rds/shortguide.pdf.

8. Can infected cattle be detected before they become ill?
Blood tests and tests on faeces are available. Although they can be useful, they are not sensitive enough to detect all infected animals.

9. Can cattle be infected with *Map* without exhibiting symptoms of the disease?
Yes. Cattle are usually infected early in life but do not usually develop signs of the disease until they are adults.

10. Is there any way of telling the difference between animals that are infected, infectious or diseased?
The diagnostic challenge of Johne's Disease is detecting sub-clinically infected animals before they start to become infectious. Animals that are shedding the bacteria in their faeces are infectious and will give a positive result on faecal culture. Some will also be positive on the blood ELISA test. Animals that are clinically diseased can be shedding billions of bacteria per gram of faeces and are almost always positive to either the absorbed blood ELISA test or faecal culture, or to both.

11. How can you spot Johne's Disease?
Map is a slow growing organism. After infection, it may be years before the infected animal becomes ill. Signs of the disease are rarely seen before two to three years of age. Generally, there is a period of reduced milk output or fertility well before the animals begin to show signs of advanced disease. These signs include persistent and profuse diarrhoea and significant weight loss, and are seen most commonly in animals between three and five years of age. Once signs of disease have developed, examination of a dung sample through a microscope is a useful way to confirm the diagnosis.

12. What should a farmer do if an animal is thought to be affected with Johne's Disease?
The farmer should contact his veterinary surgeon for advice.

13. What else can farmers do?
Farmers should take care that any animals they buy are not carrying the disease. They should ask the vendor for details of the health history of the source herd. Voluntary control and accreditation schemes are available which register herds believed to be free from the disease. These are run by two private organisations: the Scottish Agricultural College and Herdcare and operate to common standards agreed by an independent industry body known as Cattle Health Certification Standards (CHeCS).

14. Is management of Johne's Disease the best option?
Unless herd owners want to eradicate Johne's Disease so that they can sell breeding cattle many opt to manage the infection on farm. National strategic plans must emphasize the importance of on-farm management, especially on dairy farms, to reduce the incidence of new infections and contamination of land and milk. Calf rearing programs offer low cost practical means for on-farm management on dairy farms, and have additional benefits for calf health and productivity. Calf management is difficult on suckler beef units, but implementation of other measures will significantly reduce the risk of infection; these include buying in replacements from assured herds, decrease stocking density and de-intensify production systems, don't feed waste milk to calves, maintain cow hygiene, don't rear replacements within infected herds, check water sources for contamination, control potential wildlife reservoirs and avoid spreading manure infected with the organism onto land subsequently used for grazing or silage.

15. Aren't cattle with Johne's Disease likely to be culled for age before they are old enough to start shedding the bacteria?
Most infected cattle are culled before they break down with obvious disease but a large proportion of infected cattle do shed bacteria in adult life and can infect calves in the herd. In dairy herds with poor calf management and in beef herds with higher stocking rates (especially at calving), the degree of effective contact between adults that are shedding bacteria and calves is high enough to result in considerable spread.

16. What happens when Johne's Disease is diagnosed in an animal?
There is no statutory action taken, even in Northern Ireland where the disease is notifiable, therefore any action taken is up to the owner. There is no effective treatment for Johne's Disease. Cattle that exhibit clinical signs are likely to be excreting large numbers of organisms. Veterinary advice is that they should be removed from the herd and culled.

17. Is a vaccine available to control disease?
A live vaccine is available to veterinary surgeons from the Veterinary Laboratories Agency (VLA) for use in cattle and sheep. This does not completely prevent infection but, if linked to

management practices to reduce transmission, it may be expected to reduce the amount of disease occurring in already infected herds and the level of contamination of the environment with the bacterium. Work in France has shown that vaccination delays or dampens down the rate of development of the infection, the rate of shedding and possibly the rate of clinical disease. However, the vaccine may interfere with the tuberculin test.

18. Why is a live vaccine used for the control of Johne's Disease rather than an inactivated vaccine?

There is only one live vaccine authorised in the UK. This vaccine was developed in the 1940s, came into regular use in 1964 and has a product authorisation dating back to 1972. The current authorisation will expire on 30th October 2005.

The rationale behind developing a live vaccine, as opposed to a killed vaccine, containing 3 attenuated strains of Mycobacterium paratuberculosis has been lost in the intervening years. However, it was generally believed that creating a nodule of live vaccine organisms and adjuvant protected against reinfection with the virulent organism. Killed vaccines are available in other countries, but the UK Licensing Authority for veterinary medicinal products (The Veterinary Medicines Directorate) has not received any applications from pharmaceutical companies to authorise them for use in the UK.

19. Why was vaccination not considered to offer wider benefits in controlling Johne's Disease?

Although vaccination has been shown to reduce the number of clinical cases in an infected cattle herd, it does not eliminate infection or the number of animals that excrete *Map*, nor prevent the spread to other herds. Current vaccines are not good enough to use in non-infected herds in the expectation that they will prevent a herd becoming infected. Unlike many other vaccines in human and animal health, Johne's Disease vaccines do not have a good history of preventing infection unless they are administered before exposure.

Vaccination does not prevent infection from oral sources. Also, vaccination interferes with some diagnostic tests and so may hamper surveillance and make it difficult to demonstrate herd freedom from infection. Vaccinated animals have an increased sensitivity to Tuberculosis testing, and it is difficult to determine which disease the animal is testing positive for. Further, vaccinated animals test positive for Johne's Disease for long and variable periods of time after inoculation. For all these reasons vaccinated herds are not able to participate fully in market assurance programmes, disadvantaging the herd when selling breeding replacements. Work in France has also shown that vaccinated animals do break down with clinical disease and that herd breakdowns occur after several years of apparently being clear.

20. How common is Johne's Disease in the UK?

There is limited information on the level of infection in the national herd. Telephone and postal questionnaires were used to survey veterinary practices and dairy farms respectively in the 1990's. They arrived at estimates of herd prevalence of 1% and 17.5%. The differing estimates underline the limitations of these approaches in accurately measuring prevalence. An abattoir study in the South West of Britain, which identified the presence of *Map* in mesenteric lymph nodes of cows, resulted in an individual animal prevalence of 3.5%.

A statistically based survey by the Veterinary Laboratory Agency (VLA) has recently been commissioned to look at the prevalence of Johne's Disease in the UK dairy herd. The survey will start in 2005 and take about 2 years to complete.

21. Is Johne's Disease prevalence increasing in the UK?

Information from the Veterinary Laboratories Agency (VLA) and Scottish Agricultural Colleges (SAC) indicates an increase in submissions in which a diagnosis of Johne's Disease has been made over the past few years. This suggests that the disease prevalence is increasing.

22. Is Johne's Disease a problem in other countries?
Johne's Disease has a worldwide distribution. Sweden and some states in Australia are the only regions that can claim to be free from Johne's Disease based upon a reliable disease reporting system and extensive surveys.

Further information about Johne's Disease in other countries may be found in Appendix 2

Food Safety

23. Is it safe to eat meat from animals with Johne's Disease?
No reports have linked consumption of meat from animals with Johne's Disease to Crohn's Disease. The Food Standards Agency (FSA) and Department of Health have kept, and continue to keep, this matter under close review with their expert committees. There is no epidemiological or microbiological evidence to suggest that consumption of meat from animals with Johne's Disease has caused Crohn's Disease. A Republic of Ireland survey of 113 minced beef samples collected from a single meat processing plant over a 4 month period found no viable *Map*. (Reported by Dr Irene Grant, QUB, at a recent Chipping Campden Food Research Association conference). The risk to human health is neither proven nor disproven and the Food Standards Agency do not recommend any change in the current advice regarding the consumption of meat, i.e. on the basis of current evidence there is no need for anyone to change their dietary habits.

The FSA will refer this report to its scientific expert Advisory Committee on the Microbiological Safety of Food (ACMSF) for consideration. The FSA will review its advice on meat consumption and consider the need for further research in light of the outcome of the ACMSF discussions.

A recent Drinking Water Inspectorate study found a statistical association between the consumption of meat and Crohn's Disease. The study was not specifically designed to investigate meat therefore caution in the interpretation of the findings is required. Further information on this study can be found at www.dwi.gov.uk

24. Is M. *paratuberculosis* present in pasteurised milk?
A national study on the microbiological quality of cows' milk ran from March 1999 to August 2000. The results of the survey found *Map* in approximately 2% of pasteurised milk on retail sale. Similar results have also been found in surveys conducted in the USA and Czech Republic.

25. Is it safe to drink milk from animals with Johne's Disease?
A national study on the microbiological quality of cows milk was conducted between March 1999 and August 2000. The results of the survey, which found *Map* in approximately 2% of pasteurised milk on retail sale, were reported to the Advisory Committee on the Microbiological Safety of Food (ACMSF) in September 2000. The Committee noted that the risk to human health of drinking milk was neither proven nor disproven and did not recommend any change in the current advice regarding the consumption of milk, i.e. on the basis of current evidence there is no need for anyone to change their dietary habits.

The Food Standards Agency has published a strategy for reducing the levels of *Map* in milk. The strategy includes the following components:

- hygienic milking practices;

- effective pasteurisation of milk;
- reducing the level of *Map* in dairy herds.

For more information visit www.food.gov.uk/safereating/microbiology/mapinmilk/ and for more information on dairy hygiene refer to www.defra.gov.uk/corporate/rds/shortguide.pdf.

26. Is *M. paratuberculosis* present in drinking water?
A study of *Map* in distribution systems and consumers' premises completed by the Public Health Laboratory Service (PHLS), now part of the Health Protection Agency (HPA), in August 2003 did not detect the presence of *Map*. This strengthens the view that drinking water is unlikely to be a source of exposure.

27. Is it safe to consume drinking water or milk and dairy products potentially contaminated with *Map*?
A recent Drinking Water Inspectorate study found that neither drinking water potentially contaminated with *Map* or the intake of milk and dairy products are associated with a higher risk of developing Crohn's Disease.

28. Is *M. paratuberculosis* linked in any way to the organism that causes tuberculosis?
It is related but does not cause tuberculosis in either humans or animals.

Further information from the Drinking Water Inspectorate Report may be found in Appendix 3

Crohn's

29. What is Crohn's Disease?
Crohn's Disease is a long-term illness that causes inflammation in the gut. It can affect any part of the digestive system from the mouth to the anus. The parts most often affected are the ileum (last part of the small intestine) and the colon. The symptoms include abdominal pain, fever and weight loss.

30. How common is Crohn's Disease in the UK?
About one in 1,500 people have Crohn's Disease in the UK. Symptoms usually first appear between the ages of 15 and 30.

31. Why has *M. paratuberculosis* been linked to Crohn's Disease in humans?
It has been postulated that *M. paratuberculosis* has a role to play in Crohn's Disease because Johne's Disease, the disease caused by *M. paratuberculosis* in cattle, presents a similar clinical picture and some patients with Crohn's have been found to have *M. paratuberculosis* in their intestine. Clinical studies have also suggested successful treatment of some Crohn's disease patients following anti-*Map* chemotherapy.

32. How strong is the evidence of a link between *M. paratuberculosis* and Crohn's Disease in humans?
Experts worldwide differ in their opinion on whether *M. avium* subspecies *paratuberculosis* (*Map*) causes Crohn's disease or some cases of Crohn's Disease. The Advisory Committee on Dangerous Pathogens has on two occasions (1992 and 1998) concluded that a link could not be established on current evidence. A similar view was reached by the EU Scientific Committee on Animal Health and Animal Welfare who recommended increased and urgent research activity to resolve the issue. A causal link between the two conditions has yet to be proved or disproved,

however the Government is taking a precautionary approach in this area and the FSA and DH have kept, and continue to keep, this matter under close review.

Research

33. What action did the EU Scientific Committee on Animal Health and Animal Welfare (SCAHAW) recommend regarding animals infected with *Map*?

SCAHAW stated "aside from any possible link with Crohn's Disease, the development of the necessary tools to eradicate '*paratuberculosis'* from animals should also be a priority" and highlighted the need to:

- develop improved diagnostic methods
- develop improved vaccines
- obtain the complete genomic sequence of *Map*
- determine the distribution and levels of *Map* in infected animals
- experiment with time/temperature combinations of pasteurisation to see which would inactivate *Map*
- determine the survival of *Map* in the environment and the role of natural water and water supplies in transmission of *Map*
- carry out statistically robust studies on prevalence of *Map* in domestic and wild animals (both to assist future eradication programmes and to compare with incidence of Crohn's Disease)

34. Why does Defra have no ongoing research on *Map*?

In view of the absence of an established link between Johne's Disease in cattle and Crohn's Disease in humans, research on Johne's Disease was considered alongside other non-zoonotic endemic livestock diseases. A number of these are more significant, economically, than *Map* or impact adversely on sustainable development. However, some research has been maintained in Scotland by SEERAD. Defra has a large research programme on bovine tuberculosis caused by the related organism *Mycobacterium bovis*. Some of the outputs from this research will also assist in filling some gaps in knowledge on *Map*.

35. What work is Defra undertaking on the *Map* strategy?

A statistically based survey by the Veterinary Laboratories Agency has recently been commissioned to look at the prevalence of Johne's Disease in the UK dairy herd. The survey will start in 2005 and take about 2 years to complete.

Defra is supporting an initiative by the National Beef Association to raise awareness of Johne's Disease in the beef sector. Guidance to the veterinary profession will be published in September 2005 which will be the start of the industry campaign to reduce the prevalence of Johne's Disease in the GB beef herd.

36. What guidance has been given to the dairy industry?

Defra and devolved administrations launched guidance on the control of Johne's Disease in dairy herds at the Dairy Event in September 2004. Two documents were published:

- a 10 point plan, in the form of a glossy A5 leaflet giving advice about on-farm priorities, for general distribution to all dairy farmers;
- more detailed guidance notes explaining the background to the advice, to be used as a basis for discussion between veterinary surgeons and dairy farmers in setting up plans for monitoring and control.

Both documents are available on Defra's and DARD's websites. The guidance notes were distributed to all milk producers, large animal Local Veterinary Inspectors (LVIs), Animal Health Offices, Regional Veterinary Laboratories, Scottish Agricultural Laboratories and Libraries at Veterinary and Agricultural Universities.

37. What recommendations were made in the Scottish Agricultural College's Report on the surveillance and control of Johne's Disease?

The report's recommendations were divided into three headings: research, surveillance and control and included an economic evaluation:

Research

Significant deficiencies were identified in knowledge of the biology of the bacterium, the pathogenesis and epidemiology of the disease and the available diagnostic tools. These deficiencies limit the development of control strategies and the report therefore recommends further research into these areas.

Surveillance

Current surveillance systems within GB were considered to be inadequate. The report recommends validation of the ELISA test in cattle in GB, followed by national surveys of the dairy and beef herds to be repeated every 5 years. It also recommended a survey of the national sheep flock using the agar gel diffusion test.

Control

The report recommends that vaccination should only be considered as a control method in herds that do not sell stock for breeding purposes. A separate issue not dealt with in the report as it confines itself to animal health issues, is whether it is appropriate to continue to license a live vaccine in GB. The report also recommended the formation through an accredited herd scheme of a cadre of herds free from infection that can sell accredited breeding stock. Information on disease status must be made available to purchasers. The report notes that in infected herds there is no published information which demonstrates that test and cull is successful. If it is to succeed it must be accompanied by improved hygiene and management of calves. In dairy herds advice on the pooling of colostrum for feeding will contradict advice given by the former MAFF.

38. Are control costs too high to warrant action?

Useful cost-benefit indices are difficult to produce, largely because the models can not predict the rates of spread of Johne's Disease between herds under different control options.

So why opt for a National Strategic Plan?

- Though the evidence to date does not support the theory that *M. paratuberculosis* is involved in causing Crohn's Disease in people, the possibility and the concern that exists in some groups, makes it prudent to manage Johne's Disease to reduce any real or perceived threats.
- Many countries, including the UK (soon) are major traders in livestock and livestock products in a global market where several of its major markets and competitors are implementing Johne's Disease control programs.
- It is believed that the majority of herds in the UK will not be infected with the insidious, untreatable disease that Johne's Disease is and there is no advantage for them or the nation to become infected.
- Johne's Disease can cause significant mortality and shortening of planned productive lifespan, and decreased production whilst within herd, if left uncontrolled.

39. Will Defra now be considering building up a research programme on Johne's Disease?

Yes. Defra will continue to consider the need for research on *Map* in collaboration with the devolved administrations.

40. What is required to ensure surveillance of Johne's Disease is reliably carried out?
For surveillance to be effective, the first requirement is to identify a valid diagnostic test. Once a valid test has been found consideration will need to focus on what is the most efficient arrangement for undertaking the surveillance.

You can't have a successful survey without the support of cattle owners and the cattle industry.

41. How long will it be before the successful surveillance of Johne's Disease is achieved?
In view of the current deficiencies in tests for infection and in the absence of really effective preventative measures, the provision of a suitable surveillance programme for Johne's Disease will be a difficult and long term challenge.

42. How accurate are the screening tests for Johne's Disease?
There are two measures of accuracy related to how good a test is at correctly identifying infected and non-infected animals.

The ability of the Johne's Disease tests to detect infected animals (*test sensitivity*) is low because the growth of the bacteria and development of Johne's Disease in infected animals is slow. The lower the sensitivity, the more infected animals test negative (i.e., higher false negative rate). Tests for antibody in blood and for bacteria in faeces are often negative in the early stages of infection.

Work in Australia which reviewed the ELISA antibody test, concluded that, in early infection, the test detected about 20% of infections, and in advanced disease it detected 80%. On average, this review recommended a figure of 30%. A more recent modelling analysis of the Victorian program has suggested that the sensitivity in sub-clinically infected cows, mostly in seasonal dairy herds, may be even less than that. If the test sensitivity is lower than currently accepted, this would have significant knock-on effects for how the ELISA is used for surveillance, control and assurance. Tests with low sensitivity in individual animals can still be used to provide an assessment of herd status but the assurance gained from the testing itself would be lower.

The other measure of accuracy is *specificity*, or how good a test is at correctly giving negative results for non-infected animals. Johne's Disease tests are highly specific and give very few false positives. In southern Australia, the ELISA usually gives only 2-3 false positive results per 1,000 tests. Culture and histopathology should be 100% specific when conducted according to the national standard procedures (i.e., no false positives).

43. What is the Government's future policy on issues of protecting human health from *Mycobacterium avium* subspecies *paratuberculosis* in pasteurised milk?
Since small numbers of *Map* organisms have been shown to survive milk pasteurisation, the Food Standards Agency has developed, in consultation with all relevant stakeholders, a precautionary strategy to reduce human exposure to *Map* via the milk supply. This focuses on a combination of initiatives in the milk production and processing chain because a single measure that could be quickly applied to control *Map* in milk has not been identified. Responsibility for delivery of the Strategy rests jointly with Defra and the FSA.

Appendix 1

How *Map* is spread

Work in Scotland found that *M. paratuberculosis* was common in rabbits in one heavily infected region and in animals that preyed on them, including birds. However, contamination rates by rabbits were estimated to be only about one hundredth of the contamination from infected cattle. The bacteria also infect wild deer and other ruminants in parts of Europe and North America.

Where a farm environment is heavily contaminated by faeces from infected animals, any animals and plants in that environment could be exposed to *M. paratuberculosis*. The level of exposure will influence whether the animals become infected and, in turn, become sources of further contamination.

In a heavily infected area in Scotland, where clinical cases of Johne's Disease are common and where *M. paratuberculosis* has also been found in rabbits, the bacteria have also been cultured from the guts of predators and carrion-eating birds, especially crows. The results indicated that, in such circumstances, birds could probably pass bacteria in their droppings and contaminate pasture but very few appear to actually become infected.

The bacteria survive in water for months and have been shown to survive for over a year. Where water is heavily contaminated by *M. paratuberculosis* it could lead to infection of susceptible animals that consume enough of it. So, heavily contaminated drainage from infected properties should be regarded as a real risk. The potential for long-distance spread downstream is not known but is thought to be low, as the organism is killed by heat and sunlight and has to compete with other microbes.

Appendix 2

Johne's Disease in other countries

The Netherlands and several states in the USA have had control programs operating in dairy herds for several years while Sweden, Norway and Japan are in the process of attempting to eradicate Johne's Disease. France has on-farm control programs in place. The USA also has national standards for assurance and control programs. Canada decided to take a national approach to controlling Johne's Disease in 2001.

New Zealand (NZ) is often cited as one country that is similar to Australia but is not worrying about Johne's Disease. The NZ government has deregulated its control because it considers that Johne's Disease is an endemic production disease that industry should manage as it sees fit. In contrast to Australia, the disease is widespread in NZ. An economic analysis in 1998 concluded that, for the dairy industry where 60% of herds are estimated to be infected, Johne's Disease is a significant disease, costing about $19 million per annum. The dairy industry is now looking at whether a market assurance program should be developed. The NZ deer industry is facing a mounting Johne's Disease problem with most cases occurring in young deer. The prevalence and the impacts of Johne's Disease in the beef industry are thought to be low. The NZ dairy industry is considering its options for surveillance and control and research is being conducted by MAF and universities.

In Australia Johne's Disease is only endemic in the south-eastern dairy industry and in some herds of beef cattle, goats and deer in south-eastern Australia. It is rare or absent from the great majority of the country and its herds and this restricted distribution is the major factor that is driving the national control of Johne's Disease in Australia, and has driven programs by States and Territories for many years. Johne's Disease was first identified late in the 19th century and was first recorded in Australia in an imported bull that was in quarantine in 1911. The first detection in Australian cattle was in dairy cattle in Victoria in 1925. Johne's Disease is endemic in

the south-eastern dairy industry. All the evidence to date indicates that it is uncommon in the pure beef industry, in herds where there has been little contact with dairy cattle. There have, however, been some notable exceptions where beef breeding herds have been endemically infected and, in turn, infected client's herds.

Johne's Disease has occurred in goat herds for some time but much of the endemic infection in the dairy goat industry appears to have been controlled by improved management programs for Johne's Disease (and Caprine Arthritis-Encephalitis or CAE) in the 1980s and early 1990s.

Spread has only occurred in alpaca and deer in the 1990s. The alpaca industry encouraged a market assurance approach and no Johne's Disease has been detected in alpaca in recent years. Recent spread from stud red-deer herds has caused concern in the deer industry. The deer industry has supported the development of diagnostic tests test suited to deer and a market assurance program.

There is a relatively narrow spectrum of types of *M. paratuberculosis* in Australia and these have differences in their DNA that can be distinguished in the laboratory. Historically, different strains of *M. paratuberculosis* have evolved that are primarily adapted to sheep or cattle. Although cross-infection from sheep to cattle and from cattle to sheep has been detected in Australia, research and investigations indicates that it does not occur readily. However, it is quite possible that a strain adapted to both species could evolve here if ovine Johne's Disease or bovine Johne's Disease was left uncontrolled in a mixed population. The situation will continue to be monitored to determine if it is important in the spread and persistence of infection on farms.

Appendix 3

Conclusions from the Drinking Water Inspectorate Report

What is Defra's opinion of the report?
The report is well written and carried out to a high scientific standard. It contributes to our scientific understanding of the epidemiology of Crohn's Disease, although the associations identified in the report need to be interpreted carefully. The report was subject to an independent peer review which found that it was a well conducted case-control study which adds to the knowledge of *Map* and Crohn's Disease.

What was the aim of the study?
1. To investigate a possible role for *Map* in the causation of Crohn's Disease using a case control study.
2. To determine whether individuals consuming water or milk and dairy products potentially contaminated with *Map* are at a higher risk of developing Crohn's Disease.

What were the objectives of the study?
1. To determine whether drinking potentially *Map* contaminated water is associated with the risk of developing Crohn's Disease.

2. To determine whether intake of milk and dairy products is associated with a higher risk of Crohn's Disease.

What was the primary hypothesis under investigation in the study?
The primary hypothesis was that exposure to water, milk or dairy products potentially contaminated with *Map* will be associated with Crohn's Disease.

What were the main results of the study?
The findings of this study do not support either of the two primary hypotheses that drinking water potentially contaminated with *Map* or the intake of milk and dairy products are associated with a higher risk of developing Crohn's Disease. Indeed this study represents the first observation of a negative association between higher levels of pasteurised milk intake and the risk of Crohn's Disease, an effect seen in patients with penetrating Crohn's Disease and disease of the ileocolon. In addition to the primary hypotheses, an association with farm visits or contact with farm animals was not observed. Taken together these findings do not support a causative role for *Map* in the aetiology of Crohn's Disease. An observation which is consistent with the recently reported conclusions of a randomised double blind control trial of anti-*Map* therapy for treatment of Crohn's Disease.

What other findings were there?
As expected from earlier studies, family history and smoking were both associated with increased risk in the final model. A negative association with fruit consumption and travel abroad and a positive association with meat consumption were also observed in the final model. Since the study was not specifically designed to investigate these factors, caution in the interpretation is required. However, the negative association with fruit consumption has been reported previously in more than one study, lending weight to this finding. The negative association with travel abroad was not anticipated and at present remains unexplained.

Have these associations been found in previous studies?
To our knowledge this is the first study to identify an association with meat consumption and, as this was an unexpected finding, no definite conclusions can be drawn. Further work is therefore warranted to confirm this association since unexpected findings such as this can arise by chance. If the association with meat consumption is confirmed, this may in fact be related to total protein intake rather than to an infectious agent, a finding that has already been reported previously.

Why were other factors besides drinking water, milk and dairy products considered in the study?
In a study of this type it is usual to collect information about a range of factors some of which are not thought to be related to the disease. This can help to identify any preconceptions among the participants. The additional factors included in this study were fruit; meat, (beef for example roast beef, steak, mince, stew and casserole) plus canned meat (for example corned beef); fish; cod liver oil; genetics i.e. family history; smoking, oral contraceptives and travel abroad. Meat was one of the factors not thought to be related to the disease.

What is meant by "Analysis of additional variable identified meat consumption to be significantly associated with an increased risk of developing Crohn's Disease?
It means that patients with Crohn's Disease appear to be more likely to eat meat than similar patients who did not have the disease.

What is meant by an Odds Ratio (OR) of 1.40 in the Report?
The chances of someone with Crohn's Disease being a meat eater are 40 % greater than the chances of someone without the disease being a meat eater. An odds ratio of 1 would mean that there was no link between eating meat and the disease. This weak effect should be compared with the odds ratio of 7.13 for the link between disease and family history.

What is meant by 95% confidence in the Report?
If the study were repeated 20 times, in 19 cases we would expect the Odds Ratio to fall between the same limits. In only 5 % of repeat studies would we expect the result to fall outside these limits.

What is meant by CI 1.19 – 1.67?
The figure of 1.4 given as the result for the Odds Ratio is the "best estimate". The true value is most likely to be between 1.19 and 1.67.

Does this means that meat is a cause of Crohn's Disease?
No. The study has found a statistical association between consumption of meat and Crohn's Disease. This type of study cannot prove cause and effect. The primary risk factors under investigation were drinking water, pasteurised milk and dairy product intake. All other associations observed in this study should be interpreted carefully as they could arise by chance alone. Further work would be needed to confirm this association since unexpected findings such as this can arise by chance. If the association with meat consumption is confirmed, this may in fact be related to total protein intake rather than to an infectious agent, a finding that has already been reported previously.

What is meant by "a statistical association"?
It means that the association between eating meat and having Crohn's Disease appears to be more frequent than would be expected by chance. Statistical associations by themselves do not necessarily imply cause and effect.

What is meant by meat in the DWI report?
Beef, including roast, steak, mince, stew, casserole and canned meat (for example corned beef). The canned meat category may contain meat other than beef.

Why wasn't the meat question in the survey more specific?
Several other questions were included in the survey to explore other factors that are thought to increase the risk of Crohn's Disease or affect other observed associations. These factors include consumption of several food and drink categories, farm visits, farm holidays, appendectomy, smoking, dish washing and awareness of the causes of Crohn's Disease. The questions about meat were only illustrative examples of a food stuffs not thought to be related to the disease. A full dietary questionnaire about all types of meat would have been outside the scope of the original study design.

Is it safe to eat meat from animals with Johne's Disease or infected with *Map*?
No reports have linked consumption of meat from animals with Johne's Disease to Crohn's Disease. The Food Standards Agency (FSA) and Department of Health have kept and continue to keep this matter under close review with their expert committees. There is no epidemiological or microbiological evidence to suggest that consumption of meat from animals with Johne's Disease has caused Crohn's Disease. A Republic of Ireland survey of 113 minced beef samples collected from a single meat processing plant over a 4 month period found no viable *Map*. (Reported by Dr Irene Grant, QUB, at a Campden and Chorleywood Food Research Association Conference in June 2005.) The risk to human health is neither proven nor disproven and the Food Standards Agency do not recommend any change in the current advice regarding the consumption of meat, i.e. on the basis of current evidence there is no need for anyone to change their dietary habits.

The Food Standards Agency (FSA) will refer this report to its scientific expert Advisory Committee on the Microbiological Safety of Food (ACMSF) for consideration. The FSA will review its advice on meat consumption and consider the need for further research in light of the outcome of the ACMSF discussions.

What further studies are we proposing?
The results from this study will be considered in the light of others presented at the International Colloquium on Paratuberculosis that is being held in Copenhagen in August. Defra will work with the Devolved Administrations, Food Standards Agency, Department of Health to consider what further studies are necessary.

What is the relevance of dividing Crohn's Disease into different types?
Because some experts believe that the different types of Crohn's Disease may have different causes.

Why is a live vaccine used for the control of Johne's Disease rather than an inactivated vaccine?
There is only one live vaccine authorised in the UK. This vaccine was developed in the 1940s, came into regular use in 1964 and has a product authorisation dating back to 1972. The current authorisation will expire on 30th October 2005.

The rationale behind developing a live vaccine, as opposed to a killed vaccine, containing 3 attenuated strains of *Mycobacterium paratuberculosis* has been lost in the intervening years. However, it was generally believed that creating a nodule of live vaccine organisms and adjuvant protected against re-infection with the virulent organism. Killed vaccines are available in other countries, but the UK Licensing Authority for veterinary medicinal products (The Veterinary Medicines Directorate) has not received any applications from pharmaceutical companies to authorise them for use in the UK.

Could the use of a live vaccine be connected with finding *Map* in meat?
This is highly unlikely. In the UK only a relatively small number of doses are used annually. In 2004 only a few thousand doses were sold and over 50% of the doses were used in goats, not a significant meat producing animal in the UK. The characteristics of the vaccine organisms would suggest that the likelihood of extensive dissemination from the site of vaccination and reversion to virulence of the vaccine strains is remote. The vaccine is administered by subcutaneous injection and at slaughter the nodule produced at the site of injection would be removed and would therefore not be found in the meat.