24 January 2019

Geoff Gwynn
MPI *Mycoplasma bovis* Directorate

Dear Geoff

Please find attached the review by the technical advisory group (TAG) to MPI on the *Mycoplasma bovis* 2017 incursion.

The TAG has reviewed the documents and presentations given to us in late November 2018. While we understand that the scope of our work is primarily technical, we have commented on issues such as communication, social licence and staff fatigue. We have done so as we consider these as potential factors that may slow or derail eradication. This holistic approach is consistent with previous advice from the TAG.

The data presented remains consistent with a single source of introduction within the last four years. The genomic studies on isolates from around a third of the herds supports a close relationship amongst these isolates and the molecular clock analyses support a relatively recent introduction into New Zealand. The small number of newly detected herds following six rounds of bulk milk testing by PCR, and three rounds of testing by ELISA, support the assumption that there is not widespread, unlinked disease in the dairy herd population. Given the data provided, the TAG is more confident now, than in mid-2018, that eradication is achievable

Successful eradication remains critically dependent on a clear definition of the expected outcomes, a functional NAIT system, ongoing support from the farming community and other stakeholders, clarity around the prevalence and incidence of *M. bovis* in the beef industry, and ongoing availability and retention of appropriately skilled people to ensure operational success.

Communication to stakeholders about the extended timeline that will be required to ultimately declare freedom from disease, the complexity of decision-making about the status of individual farms given the current limitations of available tests, but also reassurance that eradication remains feasible despite the imperfect tests and tracing data, is required on an ongoing basis.

The TAG commends the hard work of the MPI team, and the others involved and acknowledges the remarkable effort involved, including, for example the successful completion of multiple rounds of bulk milk testing over 2018.

The TAG is happy to clarify any points in this report and remains available to provide feedback and review as and when required.

Yours

Scott McDougall
Chairman *Mycoplasma bovis* Technical Advisory Group

Technical Advisory Group *Mycoplasma bovis* 2017

Review of response progress and recommendations

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24 January 2019

1. Executive Summary

- The Technical Advisory Group (TAG) for the *Mycoplasma bovis* incursion reviewed the progress of the response in late November 2018.
- The epidemiological and phylogenetic data presented support the conclusion that the current incursion is of relatively recent origin (i.e. likely sometime in late 2015/early 2016) and that there was one source. Despite extensive testing in the dairy industry, there is no evidence of the presence of unrelated *M. bovis* isolates, although a small number of infected premise (IP) herds are yet to be connected to the network. These herds may be linked by unrecorded movements. The low number (n=3) of dairy herds newly detected by polymerase chain reaction (PCR) in Spring 2018 after 6 rounds of testing provides evidence that, within the dairy industry, the incursion is delimited and described.
- Further, as yet undetected, infected dairy herds are very likely to be present after the introduction of service bulls in spring and summer 2018, and the return of 2017-born dairy animals from grazing into dairy herds in spring 2019. These herds will hopefully be found by ongoing tracing and by bulk milk surveillance.
- The prevalence and incidence within the beef industry remain unknown and although likely to be low, potentially remain a source of infection. There is an urgent need to design and implement an effective surveillance strategy for the beef industry, and to undertake a risk analysis of transmission between the dairy and beef sectors and vice versa.
- Based on the evidence presented, eradication remains technically feasible.
- It is assumed that the majority of infected dairy herds will have been detected by June 2020, and that an extended period (>5 years) of ongoing surveillance testing to demonstrate freedom from disease at industry level will be required thereafter.
- Tests to detect infection with *M. bovis* are imperfect. Serological tests based on the presence of antibody to *M. bovis* will provide greater sensitivity than tests to detect the presence of the bacteria (PCR) for detection of infected herds. Due to the low sensitivity of PCR, some herds will probably need to be declared as restricted places (RPs) and depopulated based on serological results alone. This needs to be clearly communicated in the Surveillance specifications (14 August 2018) document. The distinction between an RP and an IP is currently based on PCR testing and as an IP

is not a legally defined entity and is not useful in the response, this terminology should be discontinued. Further optimisation of cutpoints of the serological tests currently in use is achievable, and development of new confirmatory tests may provide greater clarity and hence ease in decision-making.

- Communication with affected herd owners and key stakeholders needs to be improved. Communication needs to include the rationale for eradication, the approach to eradication, testing strategies and their limitations, and that eradication remains feasible despite imperfect tracing and tests.
- Threats to eradication (in no particular order) include:
    - Lack of clarity of the end goal i.e. lack of a definition of national "freedom from disease",
    - Failure of the NAIT system to reliably capture risk animal movements with a high degree of completeness and accuracy,
    - Establishment and propagation of other *M. bovis* incursions into New Zealand, and/or infection being more widespread than currently believed.
    - Loss of social license
    - Presence of *M. bovis* in the beef industry (other than in currently known infected beef herds) without a sufficiently sensitive surveillance system for beef herds
    - Inability to resource the eradication with appropriately trained people.
    - Fatigue of staff, resulting in slow or poor decision making
- Further resources are required to undertake important strategic planning for surveillance for freedom from disease. This must include clear definitions and planning for freedom from disease surveys in both the dairy and beef sectors.
- Concerns have been raised by some farmers around the timeliness and transparency of decision-making. This may impact compliance and trust amongst the farming community. Clear and timely communication with herd owners and other stakeholders is of critical importance to the eradication campaign. Decision-making within the eradication campaign is complex because of the imperfect tests and tracing data. Thus, there is uncertainty about the true infection status of some herds. Communication and decision-making around these herds requires clarity.
- When depopulated herds are repopulated, the incoming cattle should be tested for *M. bovis* infection at the time of entry, and the herd should be tested at a later time, to validate the effectiveness of the cleaning and disinfection protocols, and to distinguish failure of these protocols from inadvertent repopulation with infected animals.

Contents

2. Recommendations

- Clearly define national freedom from disease
- Undertake strategic planning, including sampling and testing protocols pre-and post-declaration of freedom from disease
- Develop surveillance and testing strategies for the beef industry and assess possible transmission routes and likelihood of transmission of *M. bovis* from beef to dairy herds and vice versa
- Review testing protocols and test cut-offs, particularly for the bulk tank ELISA, with the aim of assessing the sensitivity and specificity of declaring herds infected based on the ELISA alone. Additionally, cut-points need to be optimised for both the bulk tank ELISA and the ELISA when used on individual animals, and the minimum cow-level seroprevalence (i.e. the minimum proportion of cows that are test positive following ELISA testing) for declaring a herd infected should be undertaken
- Form a small group of experienced clinicians/epidemiologists to provide support for the MPI epidemiology team when they are faced with difficult and complex decisions around individual farms
- Develop and implement appropriate sampling strategies following repopulation of herds to ensure that infection is not reintroduced via animals and to ensure that reinfection does not occur due to the failure of the cleaning and disinfection process.
- Continue to culture *M. bovis* from infected animals to enable ongoing whole genome sequencing and phylogenetic analyses to inform assessments of the likely timing and number of *M. bovis* incursions
- Review the use of clinical mastitis samples submitted to commercial veterinary laboratories for surveillance, with the possibility of switching to surveillance of milk samples submitted to veterinary businesses with in-house microbiology capability, which have not as yet been monitored
- Seek development of new confirmatory tests with greater sensitivity than is currently provided by PCR
- Undertake further investigation of the immunohistochemistry positive material, and consider tracing of historic potentially infected properties and of properties that have imported live cattle
- Capture disease and production data from infected dairy herds that are milking through to the end of lactation. Additionally, consider repeated sampling within these herds to determine the rate of transmission of *M. bovis*. These data are important to quantify the economic impact of *M. bovis* under New Zealand conditions, and to inform testing strategies
- Develop and implement appropriate operational metrics with the objective of minimising the interval between infection and placement of notices of direction
- Review availability of tests accessible by veterinarians and farmers outside the response to ensure appropriate sampling is undertaken and that the number of results do not overwhelm MPI epidemiology staff
- Review the scope and structure of the biophysical models
- Develop a process for ongoing assessment of compliance with NAIT
- Develop a communications plan, particularly focusing on the complexity of test interpretation, but emphasising that eradication is achievable despite imperfect tracing data, imperfect tests and other uncertainties, e.g. uncertainty about the exact

incursion date. Communication is required to directly affected farmers, farmers in general, rural professionals, and stakeholders

- MPI provide technical briefings to key stakeholders including industry, rural professionals, and other interested parties. These briefings should be provided by people with strong technical understanding of the response and the decision-making processes
- Optimise communication between Wellington-based MPI staff and those in field headquarters to provide greater clarity through to affected herd owners about the reasons for decisions and the likely timelines for further testing or slaughter
- The representation of industry at this year's meeting (Beef & Lamb NZ) was greatly appreciated and provided valuable insights for the TAG. If another meeting of TAG is held then it should include presentations from industry groups including Beef & Lamb NZ, DairyNZ, and NZVA.
- Continue to monitor the health of and, provide support to, herd owners, farm staff, MPI staff and others involved in eradication
- Ensure that there is no duplication of effort between the operational team within the directorate and the research being commissioned by the strategic scientific advisory group

3. Overview of response to date

Following the decision to eradicate in May 2018, substantial progress has been made including:

- Establishment of the *M. bovis* directorate within MPI.
- Establishment of the four field headquarters.
- Separating operational epidemiology from strategic epidemiology.
- Execution of the spring bulk tank milk surveillance testing.
- Updated phylogenetic analyses and definition of likely transmission pathways between identified infected herds, providing stronger evidence that the incursion is recent and from a single source.
- Indications that compliance with National Animal Identification and Tracing system (NAIT) is improving.

The low incidence of newly detected farms is also very encouraging.

Our expectation is that the response will continue to identify further infected herds until at least the end of summer 2020.

Although the change in organisational structure associated with the establishment of the *M. bovis* Directorate in MPI has delivered improvements in operational delivery, the TAG are concerned that there has been a loss of strategic oversight that was present twelve months ago. This could be characterised as the 'pendulum swinging too far' away from a strategic focus to an operational focus. Given the dynamic nature of any disease response process, the TAG would encourage MPI to ensure a structure that delivers operationally, but also draws upon the strategic strengths elsewhere in MPI to respond to changing demands and provide a clearer vision to staff and stakeholders. For example, there was a greatly reduced involvement of experienced Wallaceville staff during the November 2018 meeting compared to our initial meeting in November 2017 and there were no experienced veterinarians from MPI's risk assessment or animal import Directorates. Maintaining engagement with these established MPI functions is vital to ensure a broad overview informs ongoing strategy development as the response progresses.

The majority of the TAG's previous recommendations have been accepted by MPI and there has been appropriate action in response to these. However, some earlier recommendations remain relevant to the eradication programme and so these are re-iterated below:

- Resolve major deficiencies in the practical operation of the National Animal Identification and Tracing system (NAIT) and in information systems available to the Ministry for Primary Industries for managing incursions and control activities. (December 2017 TAG report)
- Maintain national surveillance for 5 years after completion of eradication, to detect any emergent foci of infection, which are most likely to arise from animals infected during the rearing phase, before first lactation. (December 2017 TAG report)
- The number of beef herds that are currently infected is probably low but there is some uncertainty about this. (April 2018 TAG report)

- Any eradication programme will need to run for at least five years and expectations should be managed such that stakeholders are not surprised when previously undetected infected herds are identified for a number of years. These will be both currently infected but as yet undetected herds, and as yet uninfected herds that have become infected. (April 2018 TAG report)
- The definition of success of any eradication or control programme should be clearly and explicitly stated in quantitative terms and agreed to by all stakeholders before the programme commences, as this will determine the design of, and commitment to, the programme. (April 2018 TAG report)
- A full eradication and surveillance plan should be developed and costed. The approach will likely differ between the dairy and beef industries. (April 2018 TAG report)
- There is a clear need to improve animal recording nationally by improving implementation, monitoring and compliance with NAIT. Additionally, messaging around biosecurity, disease identification, recording and reporting, and improved professional oversight of disease incidence on-farm are required. (April 2018 TAG report)
- The human and animal health and welfare costs are not to be underestimated and strong consideration must be given to these factors in any decision-making. (April 2018 TAG report)
- A strategy for dairy farmers to manage importation of service bulls is required. Testing of individual bulls, even repeatedly, is likely to be of low sensitivity. Thus, options include use of AI only, or some form of bull farm assurance of disease status. (April 2018 TAG report)
- Inferences from unvalidated predictive models should be viewed with caution. (May 2018 TAG report)
- The TAG has concerns that the impacts of an eradication campaign may be greater than the benefits given the current concerns over support from within the industry for an ongoing campaign and the fatigue being experienced by farmers and MPI staff. (May 2018 TAG report)

4. Detailed commentary and recommendations

a. Response indicators

The National Response Plan published on 2 July 2018 (https://www.biosecurity.govt.nz/dmsdocument/30858/loggedIn) provided eight technical and four non-technical indicators to monitor the eradication programme. A number of these are no longer relevant (for example number 4, which has a 31 December 2018 end date), and several are unnecessarily complex. Tracking the response against number of affected herds estimated from the biophysical modelling is not appropriate given the uncertainty around those models (see later).

The TAG have reviewed and updated the indicators to prompt closer review of the eradication programme. Occurrence of these indicators may inform the likelihood of success of the eradication programme. The occurrence of any one of these indicators does not necessarily mean the programme requires major change, but such occurrences should prompt careful re-evaluation of the programme. These indicators should be considered collectively. Some indicators are edited versions of the originals, whilst some have been removed because of the availability of new information, as well as the timing and maturation of the response.

Our suggested response indicators are as follows:

1. Failure to clearly define both the ultimate goal of the programme and metrics that will define this goal.
2. Infected herds are discovered where traceback does not identify a known infected herd as the source and genomic data demonstrate an absence of links to known infected herds.
3. Infected herds are detected with an estimated date of introduction earlier than the current predicted period in which incursion into New Zealand occurred and/or that are outside the current transmission network.
4. The rolling annual incidence of newly detected infected herds does not decline after March 2020.
5. The rate of occurrence of detected herds exceeds the capacity of the response team to manage these herds, as indicated by operational metrics.
6. Research or experience demonstrates that sensitivity of the national surveillance system is substantially lower than the values used in planning the system.
7. Replacement stock on multiple properties that have been depopulated and decontaminated test positive at any time AND the source of infection appears to be the farm environment.
8. The level of NAIT compliance does not improve sufficiently to allow effective tracing.

The TAG notes and supports the following existing indicators but believes they are beyond the remit of the group to provide advice on:

1. The eradication campaign loses its social licence.

2. A new and significant biosecurity response or adverse event affecting the pastoral sector occurs that requires resources to be withdrawn from *M. bovis.*
3. There are substantiated concerns that the *M. bovis* response is incurring large or long-term damage to trading agreements.

b. Assessment of progress

The TAG has been asked to provide some comment on appropriate metrics to measure the ongoing (operational) response performance. The TAG has primarily focused on biological metrics that measure performance that could affect the eradication response but has also included examples of three other metrics that may measure progress towards eradication. All but one of the biological metrics are focused on the likelihood (and likely numbers) of animals being moved off infected herds after those herds became infected, potentially resulting in transmission to new herds, and on workloads due to additional forward traces. Thus, the critical step is application of a notice of direction (NOD) to prevent further spread of disease.

Biological metrics

- Distribution of intervals from the first risk event date (i.e. the earliest date the herd may have become infected) for a herd to a decision about active surveillance.
- Distribution of intervals from first knowledge of a risk event (i.e. the first date that MPI became aware that the herd may be infected) to a decision about active surveillance.
- Distribution of intervals from the first risk event for a herd to application of a NOD.
- Distribution of intervals from first knowledge of a risk event for a herd to application of a NOD.
- Distribution of intervals from the first risk event for a herd to identification and completion of all traces.
- Distribution of intervals from first knowledge of risk event in herd to the identification and completion of all traces.
- Proportions of depopulated herds and cattle to be sampled at slaughter that are correctly sampled.

Some examples of other business performance metrics:

- Interval from detection of a high risk herd to resolution of investigation/decision about depopulation.
- Interval between depopulation and delivery of compensation.
- Staff turnover.

c. Freedom from *M. bovis* and stages in the eradication programme

A clear definition of eradication, that is, freedom from *M. bovis*, is required. This needs to include both a clear conceptual status (for example, that no *M. bovis* is present in any bovine in New Zealand) and a practical description of how that conceptual status will be demonstrated (for example, no *M. bovis* is detected by a survey designed to detect infection

in New Zealand's cattle population if more than x % of herds are infected each with a within-herd prevalence of at least y%, with at least 95% probability).

Major stages of the programme should be explicitly defined. The eradication stage will continue until New Zealand is declared free from *M. bovis*. Specific surveys to demonstrate freedom from disease will then be required. Beyond that time point, ongoing surveillance will be required for some further pre-defined period of time. These stages should be made explicit in planning and in communications with stakeholders.

The testing strategy will need to evolve as eradication changes to "freedom from disease". At the end of the response, when it is believed *M. bovis* is no longer present, test regimens with very high specificity will be required. The testing strategy, including the type of test, cutpoints and the interpretation of these need to be defined as best as possible now. It is also highly likely that the design of the programme, including the testing strategies, will be different post-eradication.

1. Communication of timelines and testing strategies is very important. There should be proactive communication of timelines and testing strategies. For example, external communications should outline the likely situation in x years and provide clear indications of how the programme, including the testing strategy, will work at that time.
2. The Government Industry Agreement will presumably include the concept of freedom and a description of how that will be demonstrated.

d. Is the surveillance strategy appropriate for the stage of the response?

i. Bulk tank milk surveillance

1. Objective evaluation of cutpoints

The ELISA cutpoints currently being used are those provided by the manufacturers. These cutpoints may not be optimal for New Zealand conditions for bulk tank milk or individual cow testing. The TAG suggests that, because more data are now available on the performance of the IDVet ELISA, it would be appropriate to use these data to assess the most appropriate cut-off for positivity in bulk tank milk samples for this stage of the programme.

2. Differences in data between laboratories. For logistical reasons MPI is subcontracting laboratory work to external laboratories. Quality assurance programmes have been put in place. Review of data presented suggests substantial differences in test results where the same samples have been tested in different laboratories. While differences in dichotomised results between laboratories could be due to S/P ratios from different laboratories falling variously to just one and the other side of the cutpoint, there is some evidence of marked differences in S/P ratios between laboratories. So further quality assurance work is required to ensure consistency of methodology amongst laboratories, as well as ongoing and routine assessment of results.

3. The current bulk tank milk surveillance strategy is based on 6 x fortnightly testing using real time PCR and 3 x monthly testing using ELISA. This testing was timed to commence approximately four weeks after the first supply of milk by a farm in spring 2018. This strategy likely optimises the sensitivity of the testing regime for spring calving herds, i.e. the expectation is that both measurable antibody titres and the presence of the organism are more likely in cows in the post-partum period. However, this strategy will be less effective for year-round or autumn calving herds. PCR screening has detected only 3 positive herds, while ELISA testing has detected >50 potentially infected herds (based on an S/P ratio > 0.3). The TAG supports the proposed change to ongoing nationwide monthly bulk milk testing by ELISA alone, but this should commence only after the bulk tank milk ELISA test has been optimised.

ii. Response surveillance (testing in herds because there is some evidence of infection)

1. Under section 2.3.2 of the Surveillance Specifications Including Tracing & Casing (14 August 2018), a herd can only be defined as an IP where there is a positive PCR test. Thus, a herd identified via trace forwards or by bulk milk surveillance that has a high prevalence of ELISA positive animals cannot be defined as an IP until a positive PCR result is obtained. Given the low sensitivity of PCR, negative PCRs are very likely in infected herds and so repeated negative PCRs should not be interpreted as absence of infection where trace forwards and/or ELISA results suggest infection may be present. Currently herds are being defined as 'testing in progress' for extended periods of time while animals are tested by PCR. These delays are causing substantial problems.

2. Thus the TAG recommends that the current criteria for defining a herd as an IP be re-evaluated based on currently available data about test performance (and especially data on the specificity of the IDVet ELISA). The serology and PCR data should be modelled to assess the proportion of uninfected herds that would be declared as IPs if the declaration criterion was a high prevalence of seropositive animals, i.e. PCR positive results are not required. This would inform the positive predictive value of such declarations, i.e. the proportion of herds so declared that are, in fact, infected. For example, consideration could be given to defining herds as IPs where either the first round of ELISA testing finds a herd level prevalence of at least XX% in trace animals and/or at least YY% amongst in-contact animals and/or, with the same animals tested repeatedly there is serological evidence of transmission within the herd, i.e. seroconversions in initially seronegative animals that are retested. The criteria for evidence of transmission within the herd could also include consideration of the direction and magnitude of changes in S/P ratios of individual animals on re-sampling (in addition to dichotomising S/P results). For herds detected via bulk milk surveillance in the absence of specific trace-forward animals, a prevalence of ELISA-positive animals of >XX% or evidence of transmission within the herd would also result in the herd being defined as an IP. This approach will allow more rapid resolution of the status of a herd where initial PCR testing fails to identify positive animals. Clarification of the sampling strategy for individual animals is also required. The current strategy of retesting previous ELISA-positive animals in a herd is due to a wish to confirm the original test, and because there has been a focus on the cumulative proportion of animals that test positive. However, this reduces the number of initially

ELISA-negative animals that are retested, so reducing the probability of detecting seroconversions. The sampling strategy should instead be optimised to focus on detecting evidence of transmission, that is, evidence of seroconversion within the herd.

iii. Testing of properties that rear calves

1. The TAG supports regular testing of properties that rear calves due to the perceived high risk of such operations. Use of legal powers should be considered to ensure an adequate sample size is achieved at each test. The benefits and costs of testing more frequently than annually should be considered.

iv. Mastitic milk surveillance

1. Since commencement (2017) until 16th November 2018, 13,978 milk samples from 2,361 farms have been tested by *M. bovis* PCR without any positive results. The TAG acknowledges the value of this attempt to find infected properties but, with the maturation of the national surveillance programme, recommends that this surveillance be ceased. However, it is noted that the recent examples of PCR positives being reported from milk samples submitted from recurrent clinical mastitis cases demonstrates the value of herd owner or veterinarian collected samples in surveillance.

2. An alternative approach would be to test milk samples from a different sub set of herds – i.e. mastitis samples from private veterinarians who perform in-house culturing which hence have not been tested by PCR. These could be sent to NZVP/IDEXX, Gribbles or SVS for *M. bovis* PCR testing. This additional testing would need to be funded by the response and private veterinarians would need to obtain written consent from herd owners. However, this surveillance strategy is likely to be less effective than other proposed strategies and is regarded as a lower priority.

v. Beef surveillance

1. Key conclusions:

Discussion and agreement around approaches to risk and surveillance within the beef industry are required amongst key stakeholders including MPI, industry representatives and epidemiologists. Five interacting issues require addressing:

- Likelihood of transmission between beef and dairy sectors
- Strategies to reduce the likelihood of transmission between beef and dairy sectors
- Surveillance options in beef herds and the overall sensitivity of various combinations of these
- Definitions of freedom for the beef sector, which for pragmatic reasons may have to be less stringent than for the dairy sector
- Evidence about herd- and animal-level prevalence's in the various types of beef herds

These five issues interact, and so should be considered jointly. It is highly likely that compromises will be required between probability of detection of infected beef herds and expense. Discussions and planning for beef surveillance should be informed by various quantitative pieces of work, as outlined below, and should involve all major stakeholders.

This planning must consider different strategies for surveillance such as estimating the current prevalence of *M. bovis* infection within beef herds versus detection of infected beef herds versus demonstration of freedom from disease at a late stage of the eradication campaign.

The TAG acknowledges that there are substantial logistical issues in testing beef herds, particularly in more extensive cow-calf operations. Substantial resources are likely to be required for beef surveillance.

2. Transmission between beef and dairy sectors

Formal risk analyses are recommended to provide better estimation of the likelihood of transfer of *M. bovis* from the beef sector to the dairy sector, should *M. bovis* be present at various prevalence's in the beef industry, and from the dairy sector to the beef sector. The former may be assisted by testing a sample of beef breeding bulls entering dairy herds.

Strategies to reduce or mitigate the likelihood and risk of transfer of *M. bovis* from the beef sector to the dairy sector and from the dairy to beef sectors, should be considered, as should strategies relating to transfer of *M. bovis* from the dairy to beef sectors. To facilitate these actions, it is a high priority to increase compliance by bull leasers with NAIT.

Formal risk assessments for both entry of *M. bovis* to the beef industry and movement from the beef industry to the dairy industry should be undertaken. These should guide development of appropriate surveillance strategies. As part of this process, high-risk operation categories (likely to include bull leasing operations and beef finishing units that aggregate animals from many sources) should be identified.

3. The status of *M. bovis* in beef herds is considered important because:
    a. Risk of transmission from beef breeding herds to dairy herds via leased or purchased beef service bulls represents a threat to the dairy industry.
    b. Risk of infection of dairy herds by co-grazing of beef finishing and dairy heifers (such as in adjacent paddocks) represents a threat to the dairy industry.
    c. Low prevalence's of infection in beef breeding herds could be an important constraint to eradication of *M. bovis* from New Zealand, because of the difficulty in surveying this sector.
    d. There is a possibility that beef herds were the sources of infection of s 9(2)(b) (ii). However, this is considered a low probability and there is currently no evidence to support this hypothesis.

4. At a basic level, the beef populations considered here based on production type are:
    a. Beef breeding herds i.e. cow-calf operations
    b. Beef finishing herds: non-breeding; grow/fatten cattle for slaughter after sale from this or subsequent properties; may receive cattle from beef breeding herds, as well as male calves from dairy herds; includes pasture-based and feedlot operations.

c. Beef bull leasers: lease or supply bulls to dairy herds (these bulls do not usually return to beef breeding herds).

5. For simplicity, we assume each beef operation herd is in just one of the categories above. Consideration will be required for herds with multiple production types, beef herds not fitting any of the above categories, beef herds that are also dairy herds, dairy support operations (that is, properties that rear and often manage mating of dairy replacement animals from weaning or 9 months of age through to a few months before first calving), and calf rearing herds (herds that grow pre-weaned calves, most commonly calves from dairy herds, in separate businesses from dairy herds), and herds changing production type over time. We use the term 'aggregator' to describe any herd that routinely receives cattle from numerous sources for management at one location. Some beef finishing herds (including feedlots and some pasture-based operations), some bull leasers, and some calf rearing units would be considered aggregators. For beef sector surveillance, those aggregators that receive cattle from beef breeding herds are of primary interest. Bull leaser aggregators and calf rearing unit aggregators could also be helpful in surveillance for *M. bovis* in dairy herds.

6. Surveillance of beef herds is currently constrained by an inability to completely identify herds, herd production types, herd sizes, and individual animal movements to and from beef herds. However, as there are interactions between the dairy and beef sectors, at least some beef breeding herds could be currently infected. To date, there has been no surveillance for *M. bovis* in beef breeding herds other than passive surveillance based on managers' observations for clinical signs. However, the apparent absence of clinical signs attributable to *M. bovis* in beef breeding herds should not be taken as evidence that the herd-level and animal-level prevalence's in this population are low.

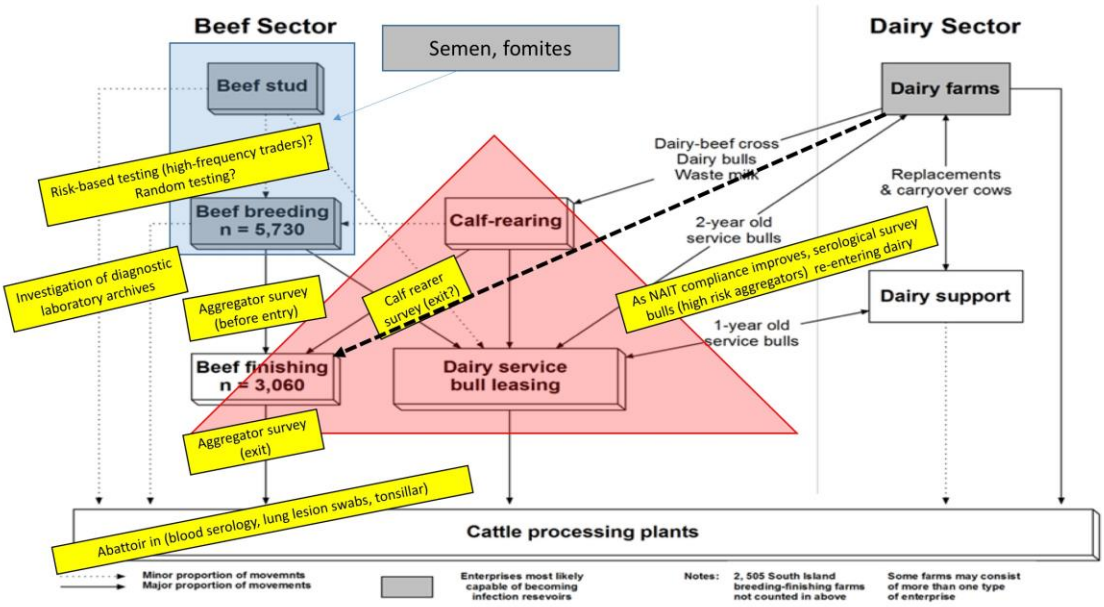
7. Potential routes through which *M. bovis* could enter beef breeding herds units from dairy herds include movement between calf rearing and beef breeding herds, fomites/human contact, return of animals to the herd following calf clubs or showing of breeding cattle, and semen.

8. Likelihood of *M. bovis* transmission and sustained infection in aggregator beef finishing herds is considered high because of the frequent introductions of beef-origin calves from numerous sources and/or dairy-origin calves (male dairy calves raised for dairy, or female dairy calves alongside beef-origin calves in co-grazing units) from numerous sources.

9. In this section, we identify a number of possible strategies that could be used for surveillance of the beef sector. An overview is provided in Figure 1. Several of these strategies could be used concurrently to increase the probability of identifying infected beef herds, particularly beef breeding herds. The overall sensitivity of various combinations of these surveillance options should be estimated using existing modelling methods. For all options chosen for implementation, strategies to distinguish likely infected herds from likely false positive herds should be clearly specified in advance. It would be useful to estimate the specificity of the animal-level ELISA in beef herds. In this section, we distinguish between efforts to identify infected herds (which is done during the eradication phase) and activities to declare the country free from *M. bovis* (i.e. proof of

freedom - activities that would be implemented after it is believed that the country is free of *M. bovis*). Finally, surveillance of beef herds may need to change over time as *M. bovis* is eliminated from the dairy sector. For example, it is assumed that infection is currently more frequent in operations finishing calves of dairy origin than in those finishing calves from beef breeding herds, but this would be expected to be reversed as *M. bovis* is eliminated from the dairy sector.

Figure 1. Possible routes of transmission of *M. bovis* between the beef and dairy industries and vice versa.



Ten possible strategies that could be used for surveillance of the beef sector are as follows:

a. Direct sampling of all beef breeding herds (i.e. using a census approach to sampling).
   i. Within each management group in each herd, an appropriate number of animals would be sampled (blood for ELISA and possibly a nasal swab for PCR).
   ii. As the likely animal-level prevalence in infected management groups is low, a large sample size would be required from each management group.
   iii. This option would provide greatest confidence of detection of *M. bovis* before transmission to dairy herds or other beef herds.
   iv. This option would be expensive for both MPI and the beef sector.

b. As above but with a random approach to sampling (i.e. testing in only a randomly selected subset of herds)
   i. This strategy could be used initially to provide empirical information about the herd- and animal-level prevalence's in beef herds.

c. As above but with a risk-based approach to sampling (i.e. testing in only a selected subset of herds that sell large numbers of consignments to other herds (i.e. not for immediate slaughter))

d. Abattoir surveillance sampling of high risk carcasses

i. Identify slaughtered animals that have lung lesions (i.e. any bronchopneumonia) or joint lesions, and selectively test these animals by PCR on samples of lung or joint lesions (and tonsil if available), and ELISA on blood (obtained from the heart chamber). As an analogy, despite the difficulty in detecting chronic lesions, the most sensitive method used during the eradication of contagious bovine pleuropneumonia, another mycoplasmal disease of cattle, from Italy (1990-1993) was abattoir surveillance by inspectors familiar with typical lesions.

ii. This (and the two abattoir surveillance strategies below) require that offal from each animal is linked to the herd NAIT number.

e. Abattoir surveillance with random sampling of carcasses

i. There would be an accumulation of numbers of animals from each herd over time, but this strategy is likely to have low herd-level sensitivity except in large herds from which many animals are processed.

f. Abattoir surveillance with risk-based sampling (i.e. sampling of animals from herds with high risk demographic or movement characteristics)

i. This would be very difficult logistically.

g. Aggregators, with cattle tested on entry

i. For surveillance of beef breeding units, beef finishing herd aggregators could be identified and cattle arriving at these herds tested on entry.

ii. Numbers would accumulate over time from individual beef breeding herds, but this strategy is likely to have low herd-level sensitivity except in large herds with many animals entering the aggregator.

iii. Such an approach would allow identification of previously unknown infected herds that were providing animals to the aggregator.

h. Aggregators with cattle tested weeks to months after entry, or at exit prior to slaughter.

i. This strategy is based on the assumption that undetected infection in beef breeding herds would eventually spread into beef finishing herd aggregators, and transmit, possibly extensively, amongst in-contact animals in those beef finishing herds.

ii. It would be useful only after any current *M. bovis* in the beef finishing herd aggregator was removed. This could occur under usual management (e.g. in beef finishing herd aggregators that introduce cattle seasonally and sell all stock before restocking) or after MPI-managed depopulation.

iii. This approach may be useful to identify infected beef breeding herds. Where *M. bovis* is detected in a small aggregator, all herds supplying cattle would be identified and assessed.

iv. It may also be useful for providing evidence that *M. bovis* is not present in beef breeding herds

v. Aggregators that introduce cattle only from beef breeding herds would be most useful for this strategy.

i. Contracted beef finishing herds

i. This option is a variant of the above that is created experimentally, by contracting one or more beef finishing herds to acquire beef-origin calves from many beef breeding herds in New Zealand, co-mingle these calves, and finish them for slaughter. The calves would be tested at the time of arrival to the aggregator, at one or more times while in the unit, and at the time of exit and/or at slaughter. Samples should include blood for ELISA, and tonsillar (and probably nasal and lung) swabs for PCR, with samples retained for culture and genotyping if needed. The potential for amplification or spread of infection among calves is expected to increase the sensitivity of this approach.

j. Beef surveillance based on laboratory archives

i. As highlighted by the possible historic presence of *M. bovis* based on immunohistochemistry (see below), diagnostic laboratory archives could be investigated as an approach to identifying other recent clinical cases in New Zealand cattle, as a strategy for surveillance of cattle populations that are otherwise difficult to assess (e.g. beef breeding herds). For example, *M. bovis* PCR could be performed on all submissions from beef cattle in 2014-2018 that had a pathological diagnosis of lung inflammation. This approach is targeted but exploratory and is not comprehensive or systematic.

vi. Sheep, goats, pigs and other species

1. *M. bovis* infection of sheep, goats and pigs is reported in the literature and in the laboratory case material of two TAG members. In New Zealand, kids, lambs and pigs have the potential for infection because they are fed unpasteurized cow's milk. This is directly analogous to a report of infection of pigs that were fed cow's milk (Spergser et al 2010). However, we are not aware of reports that these non-bovid species can transmit *M. bovis* infection back to cattle. Thus, it seems probable that these species are "spill-over" or "dead-end" hosts, not reservoirs for infection of cattle. A caveat is that no published studies have investigated this experimentally or under controlled conditions, to our knowledge. Transmission of *M. bovis* from non-bovid species to cattle cannot be excluded and culling these species from infected premises could be continued as a precautionary measure. Pasteurisation or acidification of bovine milk fed to kids, lambs or pigs should be considered as a mitigation strategy. Bulk milk surveillance of goat and sheep milk suppliers could be implemented using the same process as is currently being used for dairy cattle. However, test validation, particularly for the ELISA, would be required. This is a lower priority than cattle-focused surveillance but may be undertaken for market assurance reasons by the goat and milking sheep industries.

e. What further efforts should be pursued to understand the possible pathway of *M. bovis* incursion?

The TAG has not been asked to review the pathways work since our initial report. In December 2017 we commented that MPI's rapid risk assessments for *M. bovis* in bovine semen, bovine embryos, and non-bovine species provided robust assessments of the risks posed by these commodities. These reports clearly identify areas of uncertainty, indicate clearly where assumptions were made, and provide an objective and transparent assessment of risk, consistent with recognised risk analysis procedures. All three of these documents present an exhaustive review of available relevant literature. The TAG raised concerns with the limited depth of investigation in the risk pathways report that accompanied these risk assessments, especially the summary presented as Figure 4 of that report, and the subjective process that had been used to generate this semi-quantitative assessment.

The TAG is divided as to the importance or otherwise of undertaking further investigation of semen. Further work on semen may be useful and potentially could be funded from within the Strategic Science Advisory Group budgets. Semen cannot be ruled out as a pathway and detection of *M. bovis* in relevant historic batches of semen would provide evidence that this was the source of the incursion into New Zealand. However, the probability of finding viable *M. bovis* in historic batches of semen appears low given the low likelihood that straws from all potential risk batches are available for testing. Thus, failure to detect *M. bovis* in semen would not help rule out semen as the source of the incursion.

Regardless of whether historic batches of semen are examined, MPI should apply sanitary measures directed at mitigating the risk of future introduction of *M. bovis* in imported germplasm consistent with commitments under the WTO SPS Agreement. The justification for such measures is supported by the recent publication demonstrating introduction of *M. bovis* into Finland in imported semen (Haapala et al., 2018).

In December 2017 the TAG identified a number of additional hypotheses that might also explain the introduction of *M. bovis*. There were divergent views within the TAG in December 2017 about the likelihood of each of these pathways, although there was a consensus that investigations needed to carefully consider all possibilities beyond the focus on imported bovine semen.

The TAG previously advised that entry pathways could be further investigated by:

a. Bulk and discard milk surveillance nationally
b. Genotyping (MLST / WGS) all IPs, especially s isolates
c. Investigating the provenance of pharmaceuticals used in the s 9(2)(b)(ii) groups
d. Investigating the risk of entry associated with personnel with overseas links or of interest in the s 9(2)(b)(ii) groups
e. Attempting culture and genotyping of PCR-positive semen batches
f. Testing imported bovine animals

All of these suggestions, except testing historically imported cattle, have now been pursued. Our previous advice was that testing imported animals was not a high priority.

New evidence was presented to the TAG in November 2018 that there may have been a previous, but non-propagating, *M. bovis* incursion. A 22-month-old Dexter born to an imported Australian dam died of pneumonia in 2004. Retrospective analysis of *post-mortem* material using immunohistochemistry (IHC; a technique that uses antibodies to detect presence of the bacteria in tissue) suggests the presence of *M. bovis* in that animal. This 2004 IHC-positive case is thought to be unrelated to the current outbreak, although ongoing epidemiological investigations are occurring. Although the IHC test is not considered definitive because of issues with background staining, the combination of characteristic lesions along with a positive IHC test give credence to the diagnosis. Nonetheless, effort should be made to find the archived block of formalin-fixed paraffin-embedded (FFPE) tissue, and test scrolls for *M. bovis* using PCR or qPCR. If this can be done, it is important to avoid a false negative test by using methods validated for extraction of DNA from FFPE tissues and by using a PCR method designed for use on FFPE tissue.
If there had been earlier entry and propagation of *M. bovis*, it would be reasonable to expect greater genetic diversity in *M. bovis* in currently known infected herds in New Zealand. Even though the extent of genetic diversity could have been reduced by organism latency, based on currently available information, it is very unlikely that the recently reported IHC positive case from 2004 is directly relevant to the current *M. bovis* outbreak in New Zealand. Furthermore, the live animal importation pathway that explains this potential incursion is now closed.

This case illustrates the value of diagnostic laboratory case material in routine passive surveillance for exotic diseases. Even if this putative incursion pathway was self-limiting, identifying *M. bovis* in 2004 might have both highlighted the potential threat and entry pathway and suggested a method to prevent future incursions. In this light, it is notable that the case was tested for *M. bovis* using PCR in 2004, with a negative result. If this result were to represent a false negative test and if retesting with a currently validated PCR proves to be positive, then this would raise the point that any value of the diagnostic laboratory system in providing passive surveillance is highly dependent on MPI's ability to provide valid and sample-specific (i.e. FFPE) testing, either using in-house assays or by referral to another laboratory.

Another sample from an adult cow with pneumonia that died in 2015 has also tested positive to *M. bovis* by IHC. As with the 2004 case, this case is supported by a characteristic pathologic finding in combination with a positive IHC test result. Diagnosis in this case should be able to be easily investigated by PCR on FFPE tissues containing the lesions. As above, it will be important to use DNA extraction methods and an *M. bovis* PCR test that is validated for use in FFPE tissues. The current status of this herd is under investigation and is not yet known.

These two IHC positive historical cases indicate that further investigation of imported live cattle may be warranted, although (as discussed below) any other studies to examine the entry pathway beyond this should not be a priority, given the extent of investigations already undertaken into the pathways, as highlighted by the TAG last year.

Although there currently appears to be no association between these historic cases and the current outbreak, these cases demonstrate possible previous incursions of *M. bovis* into New Zealand. Testing of other historical samples based on a systematic examination of laboratory reports could be considered to further investigate the likelihood of prior incursions. The positive result for the 2004 case associated with a dam imported from Australia supports the prioritisation of investigating historical live cattle imports into New Zealand, as discussed above.

Live cattle imports from countries other than Australia ceased in the late 1990s, and there have been no importations from Australia since 2013. As imported cattle are subject to registration and permanent identification under the Biosecurity (Imported Animals, Embryos, and Semen Information) Regulations 1999, it should be a straightforward task to identify properties that have imported live cattle and test them and any in-contact animals if appropriate.

Given the increased incidence of *M. bovis* globally, the increase in antimicrobial resistance of *M. bovis* isolates (Barberio et al 2016) and the emerging evidence of semen transmission of *M. bovis* (Haapala et al 2018), MPI may wish to consult with other countries to advocate for changes to semen processing and testing of bulls supplying semen to reduce the risk of dissemination of mycoplasma species (including *M. bovis*) associated with international trade in germplasm. However, in December 2017, the TAG were told that the current outbreak was associated with a strain of *M. bovis* that showed susceptibility to routine antimicrobials used in semen preparations and we have not been provided with any information to indicate that this is no longer the case. Furthermore, a clear link between the current outbreak and semen imports has not been shown.

It is unlikely that infection with *M. bovis* would be considered suitable for inclusion on the list of diseases reportable to the OIE, so an international standard to address any risk of transmission in semen is unlikely. As discussed above, MPI's current risk assessments provide sufficient justification for New Zealand to implement sanitary measures on semen imports to effectively manage any risk associated with *M. bovis* in bovine semen.
An additional line of surveillance that may be more sensitive than semen screening could be following up on clinical cases of endometritis, infertility, vulvo-vaginitis and other evidence of reproductive tract disease in inseminated cattle. The proposed survey of imported semen used on identified IPs is of lower priority given the other higher priority items the TAG have identified. It may be appropriate for any further studies regarding the infection of bovine semen with *M. bovis* to be subject to consideration by the Strategic Science Advisory Group.

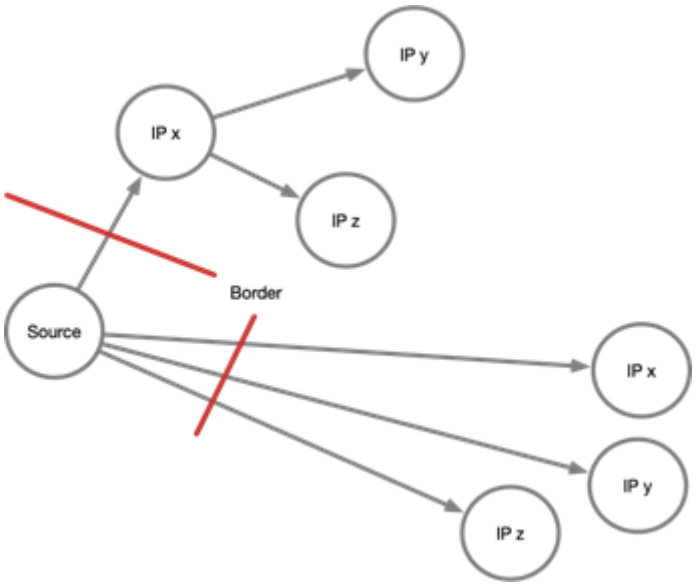
f. Does the information available, including genetic analysis, support the theory of a single recent (circa 2015) incursion?

The current genetic evidence, derived by analysis of whole genome sequence data from 171 isolates of *M. bovis* from 88 animals from 30 infected herds, indicates that the current outbreak was probably caused by recent entry into New Zealand of *M. bovis* from a single source (either a single border crossing of a single *M. bovis* clone or, potentially, up to three border crossings of three very closely related *M. bovis* clones from the same source; Figure

2). While the analyses do not enable the source to be identified, the most closely related international isolates that have been characterised are European in origin.

It is noted that the isolates tested thus far come from only about a third of the known infected places. In some cases, isolates were not recovered prior to slaughter, and/or slaughter sampling was not undertaken or was unsuccessful. It is understood that additional sampling will occur as depopulation occurs, and the TAG strongly supports further culture of samples deemed positive and whole genome sequencing of any isolates. The lack of publicly available sequence data internationally from representative *M. bovis* isolates by country is of concern and limits the ability of MPI to pinpoint the most likely source country. The TAG supports current MPI efforts to obtain more isolates and/or sequence data in an attempt to provide greater clarity and precision around the likely source.

Figure 2. Theoretical incursion pathways that would explain the current evidence for three closely related groups (clades) of *M. bovis* in New Zealand. The upper pathway represents a single historic crossing of the border of *M. bovis* followed by evolution to 3 closely related groups of *M. bovis*. The lower pathway represents the possibility that there were three crossings of the border of material from one overseas source that resulted in establishment of *M. bovis* in New Zealand.



The genomic sequence analysis and the data available from epidemiological tracing are highly coherent. Different models of the outbreak derived by integrating phylogenetic analyses of the genomic sequences and current epidemiological data are similar, providing strong support for current conclusions about the patterns of spread within New Zealand after incursion.

g. Environmental survival of *M. bovis*

M. bovis can survive in materials that can act as fomites of infection. Moreover, some organic and biological material can be viewed as reservoirs of infection in cattle. However, the strongest evidence to date is that infected cattle and their fluids are the major reservoirs

of infection and that infection is spread via exposure to that infected fluid either directly or indirectly via fomites. The only fomites with evidence for an association with transmission of *M. bovis* in an outbreak in dairy cattle are those associated with the milking process. Thus, inorganic material outside the milking system and organic/biological material such as soil, bedding, feed, etc. are unlikely to act as reservoirs of infection. Initially the authors of Transmission Risks and Ratings Version 1 of the Cleaning and Disinfection Specifications maintained a cautious approach and listed much of the material potentially associated with an *M. bovis* outbreak as having a higher risk than scientific evidence would support. The TAG supports the change in risk categorization outlined in Transmission Risks and Ratings Version 2. The increased emphasis on cattle movement as the primary transmission risk, as distinct from transmission via the environment or fomites, is supported. However, the creation of seven risk categories appears unnecessarily complex, and it is suggested that the number of risk categories be reduced to 3 (see Appendix). It should be noted that *Mycoplasma* species are sensitive to cleaning with most alkaline cleaners and to disinfectants commonly used on dairies. The Cleaning and Disinfection strategies, with associated stand down by risk category, can remain in place.

h. Infection modelling (modelling of infection transmission between herds, as distinct from economic modelling, surveillance sensitivity modelling etc)

MPI indicated that modelling is desired:

- to predict the likely total number of herds that will become infected and require depopulation over the entire eradication phase
- to predict the likely time to eradication
- to provide predicted cumulative numbers of infected herds detected by time since the start of the programme, and the numbers of newly detected infected herds per year, for comparison with actual numbers, so that the progress of the eradication programme can be monitored

Such predictions are particularly desirable given the major challenges in implementing sensitive surveillance for rapid detection of infected beef herds. These challenges could protract the time to eradication and also affect the methods of demonstration of freedom.

Three distinct types of biophysical modelling are currently being developed:

- Predictive with simulation at herd level
- Predictive with simulation at individual animal level, modelling both within and between herd transmission
- Explanatory regression modelling of potential determinants of being an IP herd, with particular emphasis on the relative importance of contact network characteristics

It is good practice to use multiple markedly different approaches to modelling. Similar inferences by different models improves confidence in those inferences. In addition,

conclusions from the various modelling approaches may inform each other. There is limited value in predictive models as a way of benchmarking progress towards eradication due to the high level of uncertainty about assumptions made in these models. However, the TAG supports within-herd modelling as a useful basis for modelling potential test strategies, and explanatory regression modelling with a focus on contact networks, to further inform risk-based surveillance (Appendix 3).

i. Economic modelling

The TAG was asked to not consider economic issues and so has not directly reviewed the economic modelling. The TAG's input has been restricted to providing limited feedback on inputs into the economic modelling, including the likely proportion of dairy herds showing clinical signs and the production losses associated with *M. bovis.* There is limited information about clinical disease occurrence and production losses due to *M. bovis* in infected herds both globally and in New Zealand specifically. Collation of clinical data and detailed monitoring of IPs that are milking through to the end of lactation before slaughter will provide more robust information on the incidence and prevalence of clinical disease, as well as estimates of production losses. These data could be used to revise the economic modelling. The aims of any further economic modelling should be clearly defined. If the aim is to evaluate the benefits versus costs of the current eradication programme compared to other responses that could have been chosen, there will be substantial uncertainty about numbers of infected herds that would have occurred under various possible responses, and some uncertainty (albeit diminishing over time) about what will occur under the current eradication programme, and this will be a major source of uncertainty for any economic estimates. Given the limitations of the predictive biophysical modelling described above, it is inappropriate to use outputs from that modelling as inputs into any economic modelling. The TAG are happy to be briefed about the details of the economic model assumptions and the bases for these, and to review these and report back at some later date.

j. What are the other possible threats to a successful response?

i. Other previous Incursions in live cattle

At the present time there is no evidence to link the recently reported IHC-positive historical cases of *M. bovis* infection to the current outbreak. However, as discussed above, these findings should prompt further investigation of historical live cattle imports to manage the (very low) risk of latent *M. bovis* infection in herds outside of the current response.

ii. Transmission from undetected infected beef herds to dairy herds

This issue is addressed in detail under 'Beef surveillance' above.

iii. NAIT failures

The ongoing failure of NAIT to provide sufficiently robust data to enable tracing to occur in a timely enough fashion to minimise further forward movement of infected animals is of concern. The New Zealand Parliament mandated the National Identification and Tracing Act in 2012 (http://www.legislation.govt.nz/act/public/2012/0002/latest/whole.html#DLM3732601). The purpose of the Act was the establishment of an animal identification and tracing system that

would improve livestock biosecurity and reduce or manage risks to human health potentially caused by zoonotic and food-borne diseases and/or residues. The Act would have the potential to support improved animal productivity, market assurances and trade. MPI was charged with administration of the Act. Clearly better compliance by the cattle and allied industries would facilitate the ability of the Ministry for Primary Industries to manage eradication of *M. bovis*. The ability to trace all animals through the production systems would help reduce likelihood of transmission of the agent. There have been several anecdotal statements suggesting that compliance with NAIT is unacceptable. In a recent report to the Ministry for Primary Industries by M. Sujau, E. Neumann and R. Morris (27 November 2018, Analysis of animal movements recorded in NAIT from 2016 to 2018. Model prediction for *Mycoplasma bovis* outbreak scale using additional NAIT data) it is stated: "The other key point, which the modelling reinforces, is that current surveillance may leave small pockets of infection because it does not adequately cover these groups, and this could result in failure to achieve national freedom, with the possibility of later recrudescence of infection." Moreover, the authors of this report state that the Agribase, FarmsOnLine and NAIT databases do not match well. A reliable database that the NAIT programme should be able to provide is very important in the eradication programme. The TAG strongly recommends that the Ministry for Primary Industries improves management of this programme to ensure better compliance (nearly 100%) with the Act, which will result in improved data quality.

1. The TAG understands that there are 30 new NAIT compliance officers appointed to target breaches in compliance.

2. Are there other opportunities to improve NAIT compliance?
   - Linking compliance to payments from abattoirs
   - Maintaining and improving animal health is critical for milk processors. Hence conditions of supply could be modified to incentivise compliance with NAIT or penalise breaches of NAIT compliance through milk payments and this could be implemented through the annual audit process.

3. There is a clear need to develop methodology for ongoing assessment of NAIT performance. This could be integrated into Rebecca Turner's ongoing work.
   - With respect to measuring NAIT compliance, the percentage of movements that were properly recorded may not be the only important measure of improvement in the system. Even if there is high overall national compliance, a small number of non-compliant producers would still be important if these were high-frequency traders or otherwise had a high risk of acquiring and transmitting infection to other herds. Thus, high compliance in such herds should be one performance criterion.

iv. There is no direct testing of repopulated IPs, apart from increased frequency of bulk milk testing. The current testing strategy would not be able to distinguish cleansing and disinfection failure from repopulation from an infected source herd. The lack of evidence about potential transmission by effluent was mitigated by the plan for testing herds after decontamination and repopulation, but the current plan to not test repopulated herds requires greater confidence that farms have been effectively decontaminated.

v. The intelligence review (6 November 2018) concludes that risk of transmission in gametes is low (Table 3 of that review). It appears that there is no restriction on movement of low risk material (including) gametes from a NOD (Table 4 of that review), although this is a permitted activity from RPs (Table 5 of that review). Hence activities such as custom semen collection or embryo transfer on a NOD appear to be unregulated under the revised risk strategy. The TAG suggests that gametes are a low but still possible transmission pathway and that movement of gametes from a NOD should be a permitted activity, rather than being uncontrolled as appears to be the case at present. This requires editing of Table 4 in the transmission risk and risk rating intelligence review of 6 November 2018.

vi. Policy has been that herds with elevated ELISA S/P ratios in bulk milk were not placed on a NOD immediately based on the bulk milk ELISA result alone. The response surveillance is moving to bleeding of individual cows as well as sampling for PCR in such herds. However, given the inevitable delay from initial identification of the herd as high risk based on the bulk milk ELISA to bleeding of individual cows, in the absence of a NOD, there is a risk of further transmission by cattle movements in the interim. Hence, the TAG supports the recent change to this policy so that where there is an elevated S/P ratio and other risk factors associated with the herd, a NOD can be applied prior to individual animal test results becoming available.

vii. Risks associated with response staffing

1. The TAG appreciates that the establishment of directorate and upscaling of staffing has happened rapidly. However, use of short-term contracts is resulting in uncertainty for individual staff members and may result in loss of key staff. Such uncertainty may increase the risk of staff burnout, with consequence loss of performance in the organisation. For example, it is apparent that there has been inadequate support for key strategic decision-making, relative to day-to-day operational decisions, and also inadequate support for those staff making decisions about actions in individual herds. (Both of these issues are discussed in more detail below.)

2. Communication between Wellington and regional-based staff needs to be improved so that decision timelines are reduced and there is greater understanding by all groups of specific herd-level decisions.

viii. Poor communication impacting on social license

1. There needs to be ongoing communication of the rationale for the decision to undertake eradication. The long-term benefits to individual farm businesses and the whole industry need to be emphasised.

2. Additionally communication is required around the limitations of test sensitivity and specificity, but also that eradication is feasible even in the presence of imperfect tracing and test performance. There is a need for better communication of the degree of uncertainty about various aspects of the incursion and eradication programme and the relative effect of that uncertainty

on the likely success of the programme. For example, we understand there has been some concern about the various estimated dates of the incursion. Knowing the exact date may help identify the pathway of introduction. However, given that this is not possible, uncertainty in the order of a few months will have no impact at all on the likely success of the programme. Risk communication is well-developed and there are likely to be methods and approaches that would be appropriate for the *M. bovis* communications. This communication is required to MPI staff, farmers, rural professionals and other stakeholders. There is a need for communication of the degree of 'robustness' of the eradication programme. A key message is that it is not essential that all components are operating perfectly. For example, despite low NAIT compliance, eradication is quite possible because x, y, z etc.

3. There needs to be communication with both the general farming community about fundamental epidemiological concepts (for example, test sensitivity and specificity), and on a one-to-one basis with managers and staff on affected farms about why specific decisions have been made about their herds. Such discussions may be complex, and some case managers may not have the background or knowledge to effectively communicate this complexity. However, there is a risk that key epidemiological staff members get distracted from other important roles by being asked to communicate more. Hence a clear communications strategy and training of frontline staff around some of these concepts is required.

4. Improvements to the response database may allow faster and clearer communication to regional HQ and through to specific herd owners.

5. The impact of the application of NODs, testing, and depopulation on individual farm businesses needs ongoing acknowledgement. This includes the economic and operational impact on farms, as well as the personal and social impact on farm businesses when they are identified as NODs, RPs or IPs. Importantly, uncertainty about the herd's future is clearly a major stressor for high risk herds and every possible step should be taken to reduce this period of uncertainty. There also appears to be a need for MPI to take steps to specifically address ostracism of managers of infected herds by other farmers and the farming community.

6. The complexity of decision-making within the response needs to be acknowledged and communicated. For example, test strategies and cutpoints may need to change during the response; there is a need to maximise sensitivity early in eradication, and then a need to maximise specificity later, when undertaking freedom of disease surveillance. Similarly, the use of the labels 'RP' and 'IP' need to be clarified, as the definition of an IP is based on a positive PCR result, but, as decisions to depopulate are apparently being made on serology and epidemiological evidence (in the absence of a PCR positive result), use of the 'IP' terminology is potentially confusing and unnecessary. The 'IP' terminology could be dropped, but the rationale for this will need to be clearly communicated.

7. Communication around the fact that, because of the low sensitivity of the tests, herds that have positive serological tests in the absence of a positive PCR result may be truly likely to be infected

8. Clear communication around requirements for compensation to be granted and timelines for this occur are required. The TAG understands that further training and resources are being provided to those charged with managing the compensation process. Improved cognizance of the farming year is required, including an understanding that contracting for purchase of stock etc. requires significant lead times.

ix. Poor animal welfare due to the programme adversely impacting on social license

The potential impact of movement controls on animal welfare needs to be acknowledged and mitigated. For example, retention of bobby calves on dairy farms that are NOD's or RP's, due to unavailability of abattoir slaughter space, adds considerable complexity and cost to farming businesses. If there is a perception that the welfare costs of movement restrictions outweigh any welfare impacts of the disease, there will be a risk of loss of social license.

x. Asymptomatic carrier animals

As a general principle, it is not unusual in an eradication programme to have infected herds where the organism and/or diagnostic tests behave in unexpected ways, resulting in delayed detection of such herds. These herds can become progressively more important as an eradication programme progresses as they may become the predominant reservoir of infection after most other infected herds are detected and depopulated. There are no empirical observations informing whether this is likely with *M. bovis*. There is a possibility that there are asymptomatic and potentially test negative animals within herds. Animals infected in sites other than the udder (and so avoiding detection by PCR in milk) and not seroconverting could theoretically cause delayed detection of such herds. *M. bovis* has been detected in tonsils, joints, tendon sheaths, the middle ear, semen, bull prepuces and other sites. The impact of such animals on probability and time to detection of infection at herd level is unknown, and there appear to be no high priority practical steps available to MPI to explore or address this at this stage. However, the possibility that such animals and herds exist is one reason that an extended period (>5 years) of ongoing surveillance will be required before testing to demonstrate freedom from disease at industry level. If evidence emerges that detection is being markedly delayed in some herds, specific strategies should be considered at that time.

k. Other matters discussed by the TAG

i. While spread to contiguous properties has not been observed, the risk of this is likely to be greater around large populations of infected animals. Therefore, the TAG supports the increased surveillance on properties adjacent to [redacted]. If depopulation of this property is delayed until all other infected properties in New Zealand are depopulated, the TAG recommends that there be introduction of control measures on this property. These

measures could include restrictions on movement and mixing of animals that are introduced at different times and/or from different sources, treatment to reduce the level of infection with, and hence excretion of, *M. bovis* and vaccination to control other pathogens that may enhance excretion of *M. bovis.*

ii. The lack of some of the required strategic planning (e.g. freedom of disease modelling, optimisation of test cut points for the bulk tank milk ELISA testing, modelling of required changes in testing strategy and cutpoints as the response moves from eradication to freedom of disease, etc.) suggests under-resourcing and/or diversion of the resources of the strategic epidemiology team into operational decision making. The separation of strategic and operational epidemiological functions is important and should be preserved.

iii. Framework for managing difficult cases (i.e. herds with some evidence of infection but whose infection status is unclear).

1. Delays in decision-making around the status of individual herds due to inconclusive test results and uncertainty within the epidemiological team about the optimal decision for these herds is creating uncertainty and discontent amongst some farmers.

2. There is a need to develop a more systematic and organised approach to making decisions on difficult cases with discrepant data.

3. Improved decision making would occur if the operational epidemiological personnel were able to confer with a group of knowledgeable and experienced individuals. This is a much preferred model to any one or two individuals being asked to decide the outcomes for complex cases.

4. It is important to communicate to stakeholders that high risk, but PCR negative herds will need to be slaughtered.

5. The criteria for depopulation need to be clearly described and can be changed over time as the situation changes and as knowledge develops.

iv. Clear boundaries between research being funded by via the Strategic Science Advisory Group and activities funded by operational expenditure need to be established and monitored. For example, optimisation and development of tests is clearly a requirement in the short term. Development of confirmatory tests should be a priority to assist in resolution of difficult cases and is thus also clearly a priority. This particular issue is clearly identified within the Strategic Science Advisory Group documents for funding. Cross membership of the TAG, Strategic Science Advisory Group and response will to some extent mitigate overlap and duplication, but resources are required to ensure explicit monitoring of this. It is beyond scope of the TAG to review the strategic science plan, but recommendations in this report should be assessed against the strategic science plan to ensure key needs of the response are met by the work encompassed by the proposed strategic science plan.

v. Are there response areas where resources are being over committed at present?

1. Lack of progress and/or lack of clarity in the scope of some of the modelling suggests that this work is of lower priority at this time point.

2. Depopulation process. The costs associated with cleansing and disinfection, particularly at slaughter plants handling stock infected with *M. bovis* have resulted in time delays, resistance from some works to handle these stock and potentially unnecessary expense. Confirmation of the new risk analysis and hence of the cleansing and disinfection specification should result in reduced complexity and cost to slaughter plants, thus increasing operational flexibility around slaughter.

vi. Some veterinarians and herdowners have been requesting access to ELISA testing outside the response. Increased testing may improve surveillance. However, if such access was granted, clear guidelines on sample size, sampling strategy (random vs risk based), communications and interpretation of test results, the legal and official (i.e. MPI) status of private test results, and processes to resolve apparent discrepancies between results generated within the response and those from private testing need to be developed and communicated. If such access was granted, the MPI epidemiology team would need to be sufficiently resourced to manage increased workloads associated with the need to assess/respond to private testing. Introduction of interlaboratory quality control procedures with private laboratories would also be required. It is also highly likely that such testing will generate lobbying of the minster and MPI staff over disagreements about interpretation of test results. In summary, allowing this access will necessitate additional MPI resourcing, and will add complexity to the programme, possibly delaying eradication. TAG note that the decision to release all negative test results from surveillance may reduce the interest in private ELISA testing but increases in MPI workload and eradication complexity should still be expected.

5. Noted conflict of interests

Ben Madin: Staff in his company (Ausvet) have been working in the epidemiology team, (BM will recuse himself from recommendations regarding the staffing of the epidemiology team).

Glenn Browning: His research group developed the assay on which the IDVet ELISA is based, and he is a consultant to the company supplying reagent for the manufacture of the IDVet ELISA. He is also a co-inventor of an attenuated *M. bovis* vaccine currently in development.

Appendix 1.

Intelligence Review – *M. bovis* transmission risks and risk ratings (11 October 2018)
The TAG agrees with the intention of this intelligence review to draw on the experience of the outbreak to identify high risk transmission pathways. The key finding of this work is that movement of live cattle or bovine milk from infected herds presents a transmission risk several orders of magnitude greater than effluent or water. There are insufficient data to further quantify this difference and any attempts to explore a quantitative approach to investigate these risk pathways should be discouraged.

The relative ranking of the risk pathways appears reasonable, although the use of a seven point qualitative scale (or 8 points if a 'zero risk' category is included) is not credible given the limited data available to distinguish between the risk pathways. The best granularity that could be achieved based on the available knowledge would be categorisation of risk pathways as either high, low or negligible; this would probably enable much clearer communication of the output of this work. These categories would then align with the proposed risk management measures of prohibited (high risk), permitted (low risk), or no restrictions (negligible risk).

Movements currently assessed to be 'extremely high', 'very high', or 'high' risk could be re-categorised as 'high risk'; movements currently assessed to be 'medium', 'low', or 'very low' risk could be re-categorised as 'low risk'; and movements currently assessed as 'extremely low' risk could be re-categorised as 'negligible risk'.

The TAG has previously been presented with MPI's rapid risk assessments for *M. bovis* in bovine semen, bovine embryos, and non-bovine species, which provided robust transparent assessments of the risks posed by these commodities – it would have been good to incorporate the findings of these earlier assessments as the basis for some of the intelligence review. Unlike these previous risk assessments, the intelligence review does not provide a transparent review of the available literature, so it is difficult to critically review the findings of this work. The intelligence review also generated some curious outputs. For example, accepting that process failures may occur, it is hard to reconcile the risk associated with *M. bovis* in milk pasteurised on farm for human consumption as being equivalent to the risk posed by unpasteurised milk for animal consumption.

The TAG recommends that the MPI risk assessment team be involved in reviewing this risk of transmission document to ensure it follows a recognised risk assessment approach.

Appendix 2: Commentary on cleansing and disinfection protocols for IPs

The TAG have been asked to review the specifications proposed for cleaning and disinfection of IPs. This subject was addressed in the third TAG report (27 April 2018) and we are unaware of any new information that has emerged since this time that may resolve previous uncertainties.

The TAG previously noted that, reflecting the general fragility of *M. bovis* and its susceptibility to disinfectants, a two stage disinfection process may be unnecessary. We also advised that when decontaminated farms are repopulated with cattle, these cattle should be frequently tested, and it should become quickly apparent if the decontamination was ineffective.

Summarising our earlier advice, there are limited data available about the survival of *M. bovis* in the environment, and we previously highlighted the ability of this organism to form biofilms, enabling survival for nearly 2 months in sponges and milk, and for over 2 years in water. *M. bovis* can survive in an environment contaminated with naturally infected milk. Survival on environmental surfaces is affected by temperature and sunlight. *M. bovis* can survive in manure for up to 236 days and in water for 23 days at 23-28°C when not directly exposed to sunlight. Survival in dairy bedding for at least 8 months has also been described.

Despite these findings, it is unlikely that the environment is a major source of infection. More generally, *Mycoplasma* species are readily killed by disinfectants and do not survive for prolonged periods outside the host. There is a vast amount of evidence in published literature to demonstrate the environmental fragility of *Mycoplasma species*. There is no published evidence that indicates the environment should be considered a significant source of *M. bovis* infection. The TAG previously noted that beginning a 60 day stand down period when the last animal leaves a property and relying on anaerobic inactivation of the organism in effluent ponds is unlikely to result in a significant increase in the likelihood of re-introduced stock being infected from the farm environment.

Reflecting uncertainty associated with limited data, the TAG previously advised that, as a precautionary measure, it would be prudent to fully restock properties only after sentinels have been introduced and tested for infection. As noted above, when depopulated farms are repopulated with cattle, these cattle should be frequently tested, and it should become quickly apparent if the decontamination was ineffective. However, it is unlikely that the environment would be a major source of infection.

To further examine the risks associated with effluent or faecal contamination of farm equipment, a formal risk assessment process could be considered. However, any such assessment would require a number of assumptions that would result in significant uncertainty.

Based on our previous advice, the TAG supports the cleansing and disinfection specifications described in the document ‘Biosecurity Response: Organism Management Specifications, Cleaning and Disinfection, 06 November 2018’.

Appendix 3: Detailed commentary on modelling

1) Handispread modelling:

Roger Morris and team had been asked by MPI to update earlier predictions from the model developed using animal-movement parameters based on 2016-2017 NAIT data (rather than earlier NAIT movement data based on modelling by Sanson and Bosson), and updated information from ongoing MPI surveillance and control activities. Other adjustments and corrections have also been made to the model since those earlier predictions.

Analysis of the 2016-2017 NAIT data has identified important and implausible differences in movement data distributions from those derived from earlier NAIT data. Of concern is the need for major changes in transmission parameter estimates, achieved through an *ad hoc* tuning process, in order to provide sensible outputs of predicted IPs given these NAIT derived movement distributions. Accordingly, resolution of these discrepancies is required before any inferences can be drawn from the model.

More generally, this predictive modelling approach involves updates with real data (numbers of herds infected, etc.) and in essence uses the recent data, along with other information and tuning of parameters, to predict the current and future progress of the incursion. Accordingly, one would expect the model predictions of the current situation and near future to be accurate, but prediction of the likely number of infected herds further into the future will be less precise, resulting in large variations in the predicted numbers of infected herds.

In addition, the variability in model predictions is of equal or greater importance than the median of those predictions. This variability was substantial in the earlier predictions, and this is likely to be the case with updated predictions and further into the future, precluding use of model predictions to precisely monitor eradication programme progress. The model may understate the true degree of uncertainty. *M. bovis* transmission between herds in a national population is highly complex, and considerable uncertainty remains about the impact of unmodeled or inappropriately modelled complexity on the robustness of model predictions. Thus, the TAG recommends that the number of herds predicted to be infected at various time points into the future by this model **not** be used as an indicator of eradication progress. There are more appropriate ways to do this, including the actual annual incidence of newly detected infected herds.

As such, the TAG concluded that this predictive modelling is of limited use in producing reliable long term predictions and so is unlikely to inform the eradication programme in any useful way.

2) Hidano et al. modelling:

The current scope of this ambitious project is to develop a tool, using simulation at the individual animal level within herds, that can be used to inform decision making, with particular reference to optimising surveillance and control. It is proposed by the investigators that the model be extended to simulate between-herd transmission based on movements generated by simulated availability of animals for sale and simulated need to introduce animals.

Our view is that this modelling project would have greater utility if focused on producing a simpler intra-herd model that can be used for specific strategic purposes. For example, the model could inform risk-based surveillance strategies by identifying which management groups within herds are more likely to be infected under various scenarios, how many animals should be sampled, the effects of herd size on *M. bovis* distribution within herds, herd dynamics that determine the likelihood of spontaneous eradication, and the seroprevalence at different times after entry of *M. bovis* into a herd in various management groups. This model could also inform the herd-level sensitivity of the bulk tank surveillance regimen under various scenarios. We would also recommend that model parameters are, where possible, informed by data generated in the current outbreak (e.g. serological data) and estimated using appropriate statistical methods.

Given the progress to date as presented to the TAG, we recommend the development of working model over a shorter timescale, based on existing, published models of infectious disease dynamics in structured cattle populations and adapted to include relevant transmission pathways associated with transmission of *M. bovis*. The aim should be to develop a simple within-herd model with relatively few parameters within 3 months. Such a model could, if necessary, be extended to add complexity. Compartmental SIR/SEIR models (deterministic and stochastic) should be considered as these can be rapidly implemented and interrogated and could save time and cost.

Other important immediate steps include the following:

- Review of the scope and design of this model
- Thoroughly review what is known about *M. bovis* transmission within herds
- Plan with MPI of the use of test results from cattle from known infected premises to inform some parameters
    - This must proceed quickly, i.e. before these herds are depopulated
    - If required, design of sampling strategies in some current IP herds prior to slaughter to inform critical transmission parameters of the model
    - It may be possible to modify the model design somewhat based on parameters that are available in the literature
- Explore potential collaboration with Liza Rosenbaum Nielsen (University of Copenhagen), as she may also be working on similar models.

3) Rebecca Turner's NAIT modelling:

This modelling approach, based on an analysis of the farm contact network, could be useful in informing identification of high risk (i.e. multiple contact) and high-spread herds (i.e. herds at risk of being infected and then spreading *M. bovis* to multiple other herds).

Use of multivariable logistic regression models at herd level may have utility in identifying as yet unidentified at-risk herds. This may be useful for the beef industry, as no surveillance has yet been undertaken in this sector. The model could further be optimised by modelling known spread events and modelling whether an IP has spread *M. bovis*. Thought is required about whether the latter group should consist of IPs that have spread *M. bovis* to multiple other herds or uninfected herds. Both control groups may be appropriate. An expanded set of putative exposure variables should be assessed, with movement and genomics-informed variables jointly assessed along with farm-level covariates, including spatial variables. The output from this work would be a set of predictors of as yet unidentified infected herds that

are at higher risk of spreading *M. bovis* to multiple other herds. The discriminatory ability of the various regression models would inform the potential usefulness of the research results for this purpose.