TAG response 17 May 2018

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On 11 May 2018 the Technical Advisory Group (TAG) were asked to comment on the following questions:

- Is the current number of IPs and at-risk properties consistent with the TAG's assumptions so far about the *M bovis* outbreak in NZ?
- Does the current number and distribution of IPs, RPs or suspect positive and at-risk properties have implications for the feasibility of eradication?
- What would be the critical criteria for eradication to not be deemed technically feasible?
- At what point would the impacts of an eradication campaign outweigh the impacts of this disease becoming established in New Zealand?

High level Summary

There is variation in opinion within the TAG as to the likelihood of success of eradication. Four TAG members now believe that given the number of new infected places (IPs) and notices of direction (NOD's), that logistically and economically eradication is no longer achievable or economically rational. Conversely six believe that eradication is technically achievable given that while the scale of the job has increased substantially, the epidemiology does not appear to have changed, and hence that with sufficient resources eradication may be achieved. However, significant caveats exist including concern about the rate of ongoing new infection compared with rate of identification of these infected places, [redacted] and serious concerns about ongoing social license and personal impacts of eradication. Were an eradication decision made, a clear review point in late 2018 is required.

Key points

- TAG has been cautious about the number of undetected IPs for some time and remain concerned over the likely number of unrecorded young stock movements that may have occurred.
- No new clusters have been identified, although there has been no active surveillance outside of the trace forward process, beyond ongoing bulk tank milk testing by PCR.
- It is not possible to reliably estimate the number of infected herds in New Zealand, although it may be reasonable to assume around 50 to 75 further infected herds may be identified from the current forward tracings. Given the limited sensitivity of surveillance outside of the trace forward process, it remains possible that the number of undetected currently infected herds may be significantly more than this.
- As all the new IPs have been found as a result of high risk forward traces, and most other routes of transmission are not being actively pursued, there is insufficient data to define whether other transmission routes have occurred. However, contiguous spread appears absent or very limited.

- The documents provided to the TAG do not provide sufficient information for detailed analysis of the epidemiology or of the modelling approach.
- Inferences from unvalidated predictive models should be viewed with caution.
- TAG has previously highlighted that *M. bovis* is not associated with human health, food safety or trade concerns. Of all the IPs identified to date, significant clinical disease has only been described on two farms, with no clinical disease associated with infection described on the vast majority of properties. However, the date of detection on most farms to date is probably considerably later than initial introduction and this may reflect poor recollection of cases of clinical disease and limited record keeping on disease.
- [redacted]
- MPI is now aware of 38 IPs, so the scale of any eradication attempt would be significantly greater than previously discussed. The resource requirements for eradication are increasing substantially to the extent that these may become constraining. Thus, while eradication may be theoretically feasible, real world logistical constraints may effectively become 'technical' constraints.
- 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.

Commentary

The TAG has been provided with updated situation reports (1st of May, 10th of May) and industry stakeholders update number 78. Additionally some emails from within the modelling group outlining some of the mechanics of their work have been provided.

These documents do not provide sufficient information for detailed analysis of the epidemiology or of the modelling approach. Thus comments below are based on the limited material provided. Moreover, given concerns discussed below regarding the limited value of mathematical modelling in the face of a disease outbreak, detailed analysis of model parameters is unlikely to be useful.

TAG has been cautious about the number of undetected IPs for some time. Following the February teleconference we noted that the likelihood of undetected spread of *M. bovis* since (possibly) 2015, the scale of tracing required, and the failure of NAIT to capture animal movements suggested successful eradication was less likely than previously discussed in December. The April report from TAG noted a variation in the degree of certainty amongst TAG members as to how many as yet undetected infected places (IPs) there may be. We noted our concern over the likely number of unrecorded young stock movements that may have occurred.

The last TAG report (27 April 2018) predicted that more infected places would be found (both currently infected herds and currently uninfected herds that subsequently become infected) as trace forwards continued to detect currently infected herds, and as further herds became infected. The stakeholder update and situation reports from 10 May 2018 confirm this, with that more infected places having been identified, the number of restricted places has increased, as has the number of new trace forwards.

As these properties were identified by the trace forward process, presumably based on high risk animal movements, it is not surprising that more RPs and IPs have been identified.

No new clusters have been identified, but as there is limited active surveillance outside of the trace forward process, other than bulk tank milk testing by PCR, which was completed in autumn 2018, and which has limited sensitivity; this is also not surprising.

Thus we are still reliant on the census bulk tank milk survey work to be done in autumn 2018 to provide assurance that there are not currently as yet undetected clusters of infected herds.

Of concern is that one of the new RPs was a dairy farm and presumably tested as part of the bulk milk PCR testing earlier in the year. This reinforces the understanding that the sensitivity of the bulk tank/waste milk PCR regimen is imperfect and, based on accumulated other evidence, is likely to be low. The results of all three rounds of bulk milk/ (waste milk) PCR testing appear not to have been completed and reported. We assumed that no further IPs have been identified this way, with all the IPs and RPs being directly associated with stock movements from the original Winton cluster. Thus, it is likely that infected herds remain undetected, if they were infected by animal or milk movements that were missed by the traceforward, and they falsely tested negative on the national bulk milk surveillance.

Summary of the situation reports

Date	IP (suspect)	RP (current)	Traces (visited)	Contiguous (visited)	Other of interest	0800 (sampled)	S122 (tested)
27/Nov	8	13	65	52			19
07/Dec	8 (2)	21 (21)	39 (36)	31 (28)	90	94 (77)	24 (16)
23/Jan	18 (2)	37 [32]	55 (36)	49 (30)	173	111 (103)	28 (21)
01/Feb	20 (7)	40 [35]	62 (36)	61 (36)	196	124 (109)	41 (32)
26/Mar	28 (6)	58 (48)	91 (68)	84 (55)	543	151 (140)	65 (63)
23/Apr	32 (6)	62 (52)	121 (70)	86 (58)	727	156 (144)	74 (68)
03/May	35 (6)	71 (55)	131 (73)	85 (65)	820	160 (152)	74 (68)
10/May	38	74	252 (99)	103 (71)	804	162 (152)	85

Responses to the specific questions posed

1. Is the current number of IPs and at-risk properties consistent with the TAG's assumptions about the *M. bovis* outbreak in NZ?

How many IPs are likely to be confirmed based on presently available data?

Reliable estimates of currently undetected infected herds are not possible. The 38 confirmed IPs (as of 10 May 2018) is within the expected number given the number of trace forwards that were still pending when this data was last reviewed in late April 2018. It is not clear what proportion of the high risk forward traces (96 as of first of May 2018) have in the subsequent 14 days been confirmed as IPs, what proportion of those farms have tests pending, and what proportion have now been tested negative. There will almost certainly be more confirmed IPs as samples are collected and as laboratory testing is completed. The number of these farms is uncertain. There are 252 high risk forward traces. It would be reasonable to expect that 20 to 30% of these will result in subsequent confirmation as IPs hence a further 50 to 75 IPs appears plausible.

Given the limited surveillance outside of the trace forward process, it remains possible that the total number of undetected currently infected herds may be significantly more than this. This uncertainty was a reason for TAG's previous recommendation for a staged process with a go/no go decision point in late spring 2018. With adequate surveillance and robust animal movement data between now and then, a lot more will be known about the distribution of *M. bovis* at that point.

Is this considerably more than we previously anticipated based on our earlier discussions of sensitivity of the surveillance strategy up until now?

If these estimates of the number of currently infected herds are somewhere near correct, then they may still be within the broad estimate that there would be less than 100 infected herds. However there appears to be an exponentially increasing number of forward traces from subsequently identified IPs. The lack of movement controls is not helping this situation.

Of the likely IPs, how many can we have some confidence in the route of spread to animals on the property?

Animal movements seems to be the major route of spread, but there is insufficient knowledge to definitively know the importance of other modes of transmission. However, if all the new IPs have been found as a result of high risk forward traces, and other routes of transmission are not being actively pursued, there is insufficient data to define whether other transmission routes have occurred. There appears to be limited investigation or surveillance that could identify other mechanisms, other than the trace forward process. Thus the trace forward will simply confirm that animal movements remain a pathway of transmission. There appears to have been investigation of the risk of contiguous spread and this appears to have been low, and there is some limited evidence that spread within heifers being reared off-farm is also limited, suggesting the greatest risk remains animal movements.

Do the modelling predictions match the observed experience?

MPI are concerned that the spread of this disease now appears to be more extensive than predicted by the modelling work being done and are trying to reconcile this. Care should be taken in relying on the output of predictive models in the face of an outbreak. For example, model results or predictions can be highly sensitive to particular input parameters and these parameters can be very poorly understood. Inclusion of stochastic processes, with uncertainty about parameter values included in the modelling and hence multiple model predictions, can help address this uncertainty. But such processes still require estimation of the most likely value for the parameter and a plausible range of values for the parameter. A formal review of the modelling (both epidemiological and economic) is required.

2. Does the current number and distribution of IPs (38), RP's or suspect positive (36) and at-risk properties (225) have implications for the feasibility of eradication?

In December 2017, when TAG first reported to MPI and there were 12 IPs, we concluded that the prospects for successful eradication would be most favourable if it proceeded rapidly. Given the large number of animal movements associated with the end of sharemilking contracts on 31 May, the TAG advised at that time that national eradication should be complete by no later than mid-May, or at least any remaining infected or suspect herds should be under strict movement control by then.

We next provided advice to MPI in February 2018, when 23 IPs had been detected. The majority of the TAG then agreed that eradication was still feasible (and desirable) although the scale of this task was now bigger and would require a sustained effort over a prolonged period. There was a minority view at that time that successful eradication remained possible but was now less certain because of significant uncertainty around the costs and benefits of this approach. The likelihood of undetected spread of *M. bovis* since (possibly) 2015, the scale of tracing required, and the failure of NAIT to capture animal movements suggested successful eradication was now less likely than previously discussed in December. There was also uncertainty as to MPI's capacity to ensure all tracing visits were completed and all infected or suspect herds placed under strict movement controls before mid-May 2018 as the TAG had previously recommended.

When we reported in April 2018, when 32 IPs had been detected, TAG believed that eradication remained feasible given the current understanding of the incursion. However, there was a degree of caution about the probability of success of eradication given the escalating requirement for resources to deal with the growing number of trace forwards, as well as dealing with a potentially substantial number of test positive herds in spring 2018, and uncertainty about unknown animal movements and unknown infected herds. To this end, the TAG strongly recommended that robust economic modelling be undertaken once eradication and surveillance planning has occurred with a clear stop/go point set once costing of eradication and surveillance are clearer.

MPI is now aware of 38 IPs, so clearly the scale of any eradication attempt would be significantly greater than previously discussed. Although eradication may still technically be achievable, there are significant technical and social caveats around this as outlined below. Additionally rigorous cost/benefit analysis is required. Currently 4 TAG members believe eradication is no longer achievable with 6 believing that eradication can be achieved.

TAG has previously highlighted that *M. bovis* is not associated with human health, food safety or trade concerns. Infection with *M. bovis* is not listed by the World Organisation for Animal Health (OIE), indicating that it is not considered to be a significant disease of livestock internationally. Furthermore, anecdotally, the OIE have shown no interest in listing this disease when it has been raised with them before.

Additionally resource requirements for eradication are increasing substantially to the extent that these may become constraining. Thus while eradication remains technically 'achievable' (i.e. the disease transmission is understood, reasonable delimitation has occurred, and tests have sufficient sensitivity/specificity and short enough turn-around times, and etc. disease can be found and removed), real- world logistical constraints may prevent this being achieved.

3. What would be the critical criteria for eradication to not be deemed technically feasible?

The TAG has taken a technical view of this question. Economic and social considerations of impact will be discussed in the next section. The question of what is technically feasible is important to understand, as we can't presume a lack of constraints.

Reasons that eradication may not be technically feasible:

- Rate of disease spread is faster than the rate of detection
- Significant incomplete tracing of infected animal movements
- Limited records of movements of waste milk that has been fed to calves and higher risk of this than currently believed
- Evidence within the NZ context that *M. bovis* is efficiently spread to uninfected farms by animal movement, particularly of young stock
- Uncertainty about whether transmission within a sales/auction barn is likely (as such exposures are not included in the tracing)
- Speed of tracing to limit further animal movements from forward traces that are in fact infected premises
- Number of forward traces relative to the capacity to effectively conduct these traces
- Increased animal movements resulting from Gypsy Day
- Constraints on testing due to lack of availability of reagents, and subsequent need to validate and implement different tests
- Poor test sensitivity
- Logistics involved in surveillance of non-milking herds

Discovery of IPs outside the known trace-forward network would reduce confidence that the scope of the network is known.

The lack of movement restrictions has hampered the ability to define the size of the outbreak as ongoing movements of undiagnosed but infected stock are likely to be continuing to contribute to the increasing size of the network. It is unlikely from data currently available that transmission of new infection has entirely ceased due to effective identification of all infected farms (i.e. imposition of NOD, RP or IP notices has probably not occurred on all truly infected farms and hence transmission to new farms is likely still occurring). Thus it is unlikely that all infected farms are now within the known networks. While no new clusters of farms have been identified through the bulk tank milk surveillance, and the whole gene sequencing suggests that it is a relatively recent introduction and likely supports animal movement as the major route of transmission between farms, the rate at which animal

movements are occurring, and hence the rate at which new farms are becoming infected remains of concern. The question is as to whether the rate of forward traces and confirmatory testing is faster than the rate of transmission via stock movements (recorded or unrecorded). As active intervention has been occurring since July 2017, and the trace forwards have grown substantially from then, the inference is that, either the rate of spread has been faster than the rate of detection, or that historic infected animal movements are still being discovered, or both. If the recently observed increase in detection of IPs is predominantly due to previously unidentified animal movements and infections prior to intervention (i.e. before July 2017), and new infections since that time are rare due to effective movement controls and education, then eradication appears achievable. This assumes that sensitivity of the bulk tank milk testing regime is high and that there are not many more undetected infections from that time. But if this represents detection of more recent and ongoing new infections despite movement controls, then eradication may not be achievable. With significant numbers of animal movements due to occur in the next few weeks, the likelihood that new infected places will be created appears to be very high.

Further, since it seem implausible that all stock movements have been accounted for, there is an increasing likelihood of undetected transmission to farms that will not be tested as part of the trace-forward program. Detection of these infected farms would rely on surveillance, which seems (based on present data) to have limited sensitivity.

Farm depopulation is ongoing for welfare reasons; however it appears to be going fairly slowly. This poses questions about the resources available to undertake this depopulation, although there was some suggestion that herds would be allowed to finish their milking season before culling. Risks of transmission from known infected herds that are still lactating or being held prior to depopulation must be managed. If MPI decide that eradication is no longer feasible, then the need to depopulate currently identified IPs should be reconsidered.

[redacted]

4. At what point would the impacts of an eradication campaign outweigh the impacts of this disease becoming established in New Zealand?

As stated above 4 of the 10 TAG members believe that eradication is no longer achievable. Of the remaining 6 members there is diversity of opinion as to when eradication is no longer feasible, and given time constraints this has not been fully explored. However all TAG members have concerns about the logistics requirements and impacts of eradication. Significant additional resource appears to be required to maintain or expand the tracing and laboratory work required to deal with the likely increased number of IPs in spring. The currently limited availability of reagents for the ELISA and hence the requirement to import and validate new tests is of significant concern. Given the existing number of known trace forwards, and the high likelihood that there will be more trace forwards as a result of current tracing activity and/or of new suspicious farms based on bulk milk surveillance in spring 2018, it is likely that a large number of ELISA and PCR tests will be required in the next six months. The TAG are interested to know if forward projections have been made about likely test requirements and some assessment of the probability that reagents (as well as laboratory

staff, and other consumables et cetera) will be available to perform these tests in a timely manner.

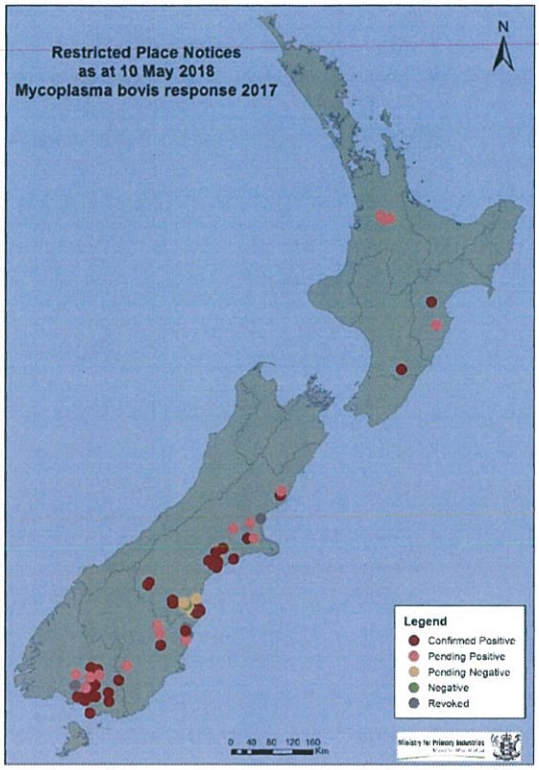
The TAG has concerns that the social impacts of an eradication campaign may be higher than the benefits, given some media reports indicating loss of support for depopulation and eradication from some farmers, and the fatigue being experienced by MPI staff. The proportion of herdowners and general public not supportive of depopulation is unclear, but will need to be managed effectively if eradication is to occur. The apparent pressure on the social licence of MPI and industry to undertake eradication is of significant concern. The anecdotal evidence is that herdowners appear to be becoming less compliant around working with MPI and industry to ensure complete disclosure of animal movements, and there is public questioning of the need to depopulate farms where there is no clinical disease, little (if any) impact on production, and no impact on trade. Were only a small number of herd owners of IPs not to disclose animal movements, and thus an increased reliance being placed on bulk tank milk or other surveillance to detect new IPs, the rate of detection of new herds may slow down substantially, allowing further animal movements to occur, and hence further spread of disease. While the degree of non-compliance is impossible to define, it is likely that the public statements by a few farmers represent only a small subset of the herd owners who may be willing to compromise eradication by not disclosing movement of stock.

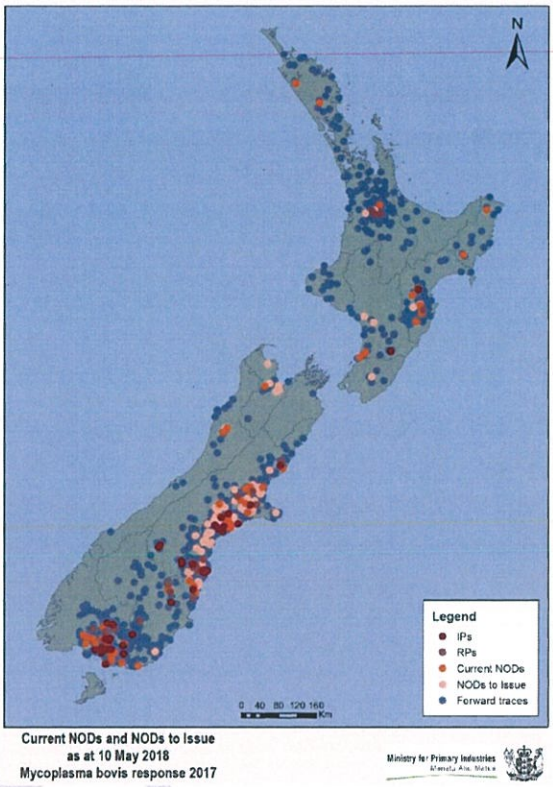
Given these impacts and the likelihood that an eradication campaign would likely need to run for 5 or more years, the TAG questions the ability to maintain support for, and compliance with, such a programme from herd owners, animal industries, government, and private veterinarians. In addition, while some demands on MPI staff may decline as an eradication program progresses, some major tasks (for example assessing surveillance positives) will continue even when few IPs remain.

Eradication of *Mycoplasma bovis* has never been attempted on national scale - so it could be argued that it is not feasible once the disease has become endemic (or even widely established). However the reasons for this are not necessarily 'technical', but rather that the impact of the disease has been deemed unlikely to exceed the predicted cost of eradication. Of all the IPs identified to date, significant clinical disease has only been described on two of the 19 farms, with no clinical disease associated with infection described on the vast majority of properties. So the critical criteria really relates to the rate of return on such a program.

[redacted]

Appendix 2. IPs, RP's, NOD's and trace forwards as at May 2018.





Current NODs and NODs to Issue
as at 10 May 2018
Mycoplasma bovis response 2017

Appendix 3. Conceptual approach to using simple SIR type models to assess rate of new infections across time.

One question the TAG has is as to the rate of new infections versus the rate of trace forwards with resultant placement of notices of direction (assuming that this will prevent further disease transmission). Use of data presumably already collected including the dates of animal movements between the date of likely infection of a herd and the date of application of the NOD, and the proportion of those forward movements resulting in new IPs would allow modelling of the incidence of infectious forward movements. This is testing effectiveness of current rate of detection and testing versus rate of new infections under the current control scenario. The graphs below represent the actual incidence of new infected places (based on analysis of the network diagram to provide the actual likely date of infection due to animal movements; blue bars) and 2 hypothetical rates of new infections (orange line).