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Executive Summary

The report reviews outputs of the JDRC modelling objective up to June 2012 and presents an extended summary of the main findings of results achieved in relation to three milestones between July 2012 and December 2013.

Milestone 5.3.9 – Effect of intervention scenarios on infection prevalence and clinical JD presented

A deer and a sheep model were developed and presented. Results suggested that two MAP genotypes tend to coexist in deer only if pathogen virulence was similar (+/- 10% virulence), else a less infectious genotype would be out-competed. Test&cull was ineffective whereas increased farmer surveillance to detect and remove young deer in clinical PTB state appeared to be an effective means to reduce prevalence. A meta-analysis was carried out to define infection parameters for the sheep model. This model considered seasonal sheep farming and yielded re-/production outputs comparable to typical NZ sheep farms. Intervention effects are described under milestone 5.3.11 below.

Milestone 5.3.10 – Mixed species sheep-cattle model developed and presented

A model of PTB in a mixed sheep&beef farm was developed and evaluated. Co-grazing two infected species, either set-stocked or by rotational grazing, increased PTB infection prevalence to a higher level than on single species farms. When set-stocked around calving/lambing for 4 months per year, naive sheep acquired infection from infected beef cattle through grazing infected pasture faster and with higher prevalence, than naive beef cattle being infected by sheep.

Milestone 5.3.11: Cost-effectiveness of intervention scenarios evaluated and presented for single species farms

**Deer:** early detection of young deer with clinical PTB was effective for reducing prevalence and likely financially attractive (due to low cost). On the contrary, test and cull (T&C) using an ELISA did not reduce prevalence. Hence T&C was neither efficient nor cost effective (more detail in 3.1.1).

**Sheep:** the annual loss due to PTB was estimated to be NZ$2.6 – 3.2 per ewe. At a population of 38m adult sheep and 75% being kept on OJD-infected farms, the total annual loss at national level would range NZ$75-92m. Vaccinating replacement lambs at weaning, the annual clinical incidence (i.e. OJD mortality) would start to decrease from 2.7% two years after starting to vaccinate and reach zero at about 9-10 years. This suggests that farmers need to maintain vaccination for an extended period before they would realise production benefits. The model further suggested that positive returns over investment were achieved if PTB caused 1.8% mortality whereas 0.75% mortality would not render vaccination as cost-effective. Hence, the critical economic threshold for vaccination was an OJD related mortality of about 1%.

**Sheep&Beef:** on mixed S&B farms, interventions to reduce PTB were more effective when applied to both species. Whereas whole herd/ELISA based T&C effectively reduced prevalence in beef cattle, it did not so in sheep. Moreover, it lasted 10 years before a notable prevalence decrease was achieved in beef cattle. Based on the high cost, T&C is unlikely to be effective. However, faecal RT-PCR based T&C may be more efficient and economical. Farmer surveillance appeared to be more effective in sheep than in beef cattle. Pasture spelling periods of more than 6 months controlled new infection rates by about 25 years after inception. Due to the slow effect and relatively long spelling periods, this does not seem to be an effective means of PTB control. Grazing sheep and beef cattle in isolation from each other could not control PTB prevalence when both were initially infected. However, in combination with increased farmer surveillance, species isolation reduced the prevalence rapidly in sheep but only quite slowly in beef. However, this combination was the most effective intervention for both species.
1. Background and Outputs up to June 2012

The report summarises outputs of one JDRC contract year 01 July 2012 to 30 June 2013. The project period was later extended until 31 December 2013. The modelling component contributes to and was informed by other JDRC research objectives using knowledge generated under Baseline Studies, Pathophysiology, Strain Typing, Diagnostics and Intervention Studies. Specific inputs to modelling were provided by Colin Mackintosh, Marian Price-Carter, Des Collins, and Geoff DeLisle (all AgResearch Ltd.).

Due to the chronic nature of PtB and the poor accuracy of diagnostic tests, the costs of longitudinal field studies to investigate infection dynamics or intervention strategies are extremely high. Mathematical modelling is a low-cost alternative to such high-input field studies. Modelling was therefore a JDRC component since inception of the programme in 2008.

Modelling outputs available prior to July 2012 addressed herd and flock prevalence of infection and incidence of clinical disease. The interaction of these outcomes with species and production type, e.g. prevalence of properties farming single versus multiple species had also been evaluated. Results were reported and published in a PhD thesis which has been forwarded to JDRC and will be available at the JDRC website (C. Verdugo 2013).

In addition to prevalence, Verdugo’s PhD thesis (2013) provided estimates of herd- and flock-level accuracy of the diagnostic protocol (PFC+ELISA). The resulting information informed industry objectives of detecting infected herd/flocks or assuring a low risk of MAP-infection assigning a ‘likely PTB free’ status. Testing 20 sheep by PFC only achieved 50% flock sensitivity (HSe) and 100% flock specificity (HSp) whereas joint testing of PFC and ELISA achieved 88% HSe and 77% HSp. Thus, PFC only would be sufficiently accurate for monitoring a ‘likely PTB free’ status (no false positive), whereas joint testing would allow the detection of MAP infected flocks. Equivalent results were obtained for beef cattle. However, the joint HSp for deer herds was as low as 37% if the Paralisa® was used for testing. As a faecal RT-PCR was not available at the time, the comparative merit of it could not be evaluated. Hence, this presents an opportunity for the future.

The statistical analysis of molecular data from the Strain Typing component generated strong inferences about inter-species transmission. The majority (80%) of MAP infected beef cattle herds carried ovine strains. Sheep and beef cattle were mainly infected with MAP Type I (ovine or type S), while dairy cattle and deer were almost exclusively infected with MAP Type II (bovine or type C). However, when beef cattle and deer were both present at farm level, infected animals tended to carry similar subtypes. Analysis of Molecular Variance (AMOVA) results indicated that the main source of subtype variation is attributable to the livestock sector (i.e. species type and combination) from which samples were sourced indicating that subtypes are generally sector-specific. Additionally, there is a relatively high degree of subtypes circulation between the two islands, since a small proportion (9%) of the total variance was found at this level. The pairwise $F_{st}$ results were similar, with low $F_{st}$ values for island differences within a livestock sector when compared to between sector analyses, representing a significant but low subtype differentiation between islands. However, for a given island, strong associations were seen between dominant subtypes and specific livestock sectors. Three subtypes accounted for 76% of the molecular variation among isolates. The most common of these was isolated from sheep and beef cattle in the North Island, the second most frequent subtype was mainly isolated from dairy cattle (located on either island), whilst the third most common subtype was associated with deer farmed in the South Island, thus accounting for overall strain type differences between islands. The PSI analysis suggests similarities in subtypes sourced from sheep and beef cattle. This contrasted with the isolates sourced from other livestock sectors, which tended to present sector-specific subtypes. Molecular typing of isolates from the Baseline Study (Massey) and from the Dairy-Genetics Study (LIC) supports that cross-species transmission of MAP occurs on New Zealand farms although close contact between species appears to be required, as for sheep and beef cattle which are commonly grazed together in New Zealand.
Modelling prior to July 2012 also addressed the transmission of MAP between farms using four years of movement data from 103 properties of Landcorp Ltd., the largest corporate farm enterprise in New Zealand. The techniques used for this purpose were Social Network Analysis (SNA) and again, molecular strain typing. SNA has the capacity to identify properties with potential high and likely low influence on the propagation of pathogens through a network of farms formed by livestock movements. This information was combined with MAP strain types to estimate whether farms connected through movements were more likely to share the same type compared to farms not or only remotely connected. This likelihood was regressed on the number of ‘path’ by which two farms were connected (e.g. 1 = two farms exchanged livestock directly, 5 = two farms had 4 farms between them in the network). It was also regressed on the physical distance (in km) between them, but this was not significant. Figure 1 shows a significant exponential association between the number of path (as simple and quadratic effect, both highly significant) and the likelihood of sharing the same MAP strain type. Results indicated that livestock movements are likely to contribute to the spread of MAP through the population of domestic ruminant livestock.

2. Specific objectives (2012/13)

The objectives were specified in the following milestones:

<table>
<thead>
<tr>
<th>Milestone</th>
<th>Description</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.3.9</td>
<td>Effect of intervention scenarios on infection prevalence and clinical JD presented</td>
<td>30 Jun 2012</td>
</tr>
<tr>
<td>5.3.10</td>
<td>Mixed species sheep-cattle model developed and presented</td>
<td>31 Dec 2012</td>
</tr>
<tr>
<td>5.3.11</td>
<td>Cost-effectiveness of intervention scenarios evaluated and presented for single species farms</td>
<td>31 Dec 2013</td>
</tr>
</tbody>
</table>

3. Results and Discussion

Mathematical models for infection dynamics and control of Ptb were developed for deer, beef cattle and sheep. The development of each model was preceded by a literature review of existing information about modelling concepts, model parameters, the patho-physiology relevant to disease dynamics, and intervention scenarios evaluated previously. It was realised that most previous models were adapted to Northern hemisphere, high-intensive, housed husbandry systems. Therefore, most information used in our models was generated from animal models of sheep (Dennis, Reddacliff, Whittington et al.) and deer (Mackintosh et al., AgResearch NZ). However, the patho-physiological process of paratuberculosis for cattle (beef or dairy) was adopted from models developed at Cornell University (Mitchell, Schukken et al.) and in France (Marce, Fourichon, Pfeiffer et al.). Work under the Modelling objective was performed in cooperation with Ynte Schukken and...
Rebecca Mitchell, and Zao Lu, all from the Faculty of Veterinary Science of Cornell University, Ithaca, NY (USA).

### 3.1 Milestone 5.3.9 – Effect of intervention scenarios on infection prevalence and clinical JD presented

#### 3.1.1 Development and validation of a deer model

A state-transition model was developed that included a susceptible (state S) and an age-dependent resistant state (state R). Susceptibility to infection was assumed to wane from 12 months of age (Mackintosh et al., 2010). Susceptible deer could become infected horizontally or vertically with sheep-type (s) or cattle-type (c) strains. They then entered either the ‘fast’ or the ‘slow’ tracks (Figure 1). Fast-track infected deer started shedding (State Y) soon after infection (Y1c,Y1s) and became high shedders/clinical within six months (Y2c,Y2s), whereas slow-track infected deer became latent (State L) infected with either cattle or sheep strains (Lc, Ls), and progressed to low-shedding (aY1c,aY1s) and subsequently high-shedding states (aY2c,aY2s) at very low rates (Table 1). The probability (ξ) of newly infected susceptible deer (S) entering the fast track was assumed to be 0.3 (Mackintosh et al 2007). The impact of all parameters on prevalence and incidence was tested in a sensitivity analysis. Parameters were modified to fit simulation results to both experimental data and survey estimates of prevalence and incidence. Horizontal transmission depended on dry matter intake (DMI), the colony forming units (CFU) of MAP organisms on pasture, and the transmission parameter (β) which encompasses both rate of contact (between susceptible animal and the environment) and infectiousness of contacts.

![Figure 2: Structure of the deer (details available at Heuer et al. 2012)](image-url)

The model intended to evaluate the persistence of single and multiple strains depending on virulence. It also compared infection prevalence and clinical incidence of PTB depending on various intervention scenarios.
In the presence of a single strain, a virulence reduction of up to 80% allowed MAP to persist in the herd ($R_0>1$). For mixed infection by two strains however, a 30% reduction in virulence of one strain was sufficient to outcompete a strain with lower virulence, suggesting that mixed infection of MAP strains with different virulence may not be common in deer (Figure 3). This finding is supported by the finding of the analysis of strain types (STs) that only few STs dominate in NZ livestock populations (ST result above). These results were similar in a 2-strain model of Ptb in sheep (presented by N Marquetoux, JDRC Science Forum, Wellington, 7 Nov 2012). The deer model showed that seasonal variation of MAP survival on pasture had little impact on transmission dynamics, and that rotational grazing with pasture spelling versus permanent grazing of the same paddock reduced both infection prevalence and clinical PTB by about 50%.

On the other hand, controlling JD by whole herd test and cull (T&C) using an ELISA did not affect prevalence at all. Reasons for the lack of a T&C effect are:

(i) The model describes true prevalence (TP) over time, not test-pos or ‘apparent’ prevalence (AP). Field observations of decreasing AP after T&C are not surprising: if the same animal group is tested a second time after the removal of test-positives, AP decreases (whole-herd testing in subsequent years would include about 80% of previous year’s animals).

(ii) At a low TP, there may be many (say 90%) false positive and few (say 10%) true test-positive among all test-positive animals, hence TP may be largely unaffected while AP decreases, simply because most removed animals had been false-positive.

(iii) Typically for T&C, many test-positive animals are being removed under T&C at the start of the programme in addition to regularly culled animals, hence more than usual young susceptible enter the herd/flock as replacements, providing ‘fuel for the fire’: the more susceptible are present, the more are at risk to get infected. In the deer model, we have described a strong effect of higher regular culling rates (in the absence of T&C) on increasing JD infection rates – for the same reason.

3.1.2 Development and validation of a sheep model

The development of a model for sheep started with a systematic literature review of existing knowledge. The objective of this work was to review studies of natural and experimental infections of sheep with MAP and use this knowledge to develop a state-transition model reflecting within-host progression of MAP infection in sheep. The evaluation of patho-physiological processes were strongly dependent on the design of the experiment (artificial versus natural challenge), the challenge dose of MAP used in the experiment, and the strain of MAP. Concerning the determination of the infectious doses based on experimental challenge, different enumeration methods for inoculum have different accuracies and are not directly comparable.

To reflect seasonal management of sheep farming, animals were subdivided into four age groups, lambs (0-3m), growers (3-12m), replacement hoggets (12-24m) and mixed age adult ewes (>24m). Figure 5 shows a model run over three years with demographic changes in these three age groups.
Lambs (red line) change into growers at weaning that are continuously marketed for meat as slaughter lambs (green line). At the end of about one year, the remaining growers are used as female replacements and become hoggets (orange line). Hoggets become adult ewes at 24m of age which then consist the reproductively active part of the flock (blue line). Seasonal lambing, culling and replacement reflect the typical reproductive cycle and management of New Zealand sheep farming.

![Figure 4: Demographic part of the model: sheep in 4 age groups (lambs 0-3m [red], growers 4-12m [green], hoggets 13-24m [orange], mixed age ewes >24m [blue]) with seasonal drafting for meat, removal and replacement. Time starts at lambing in Aug/Sep = 0-1 month.](image)

As shown in Table 1, demographic model outputs of production and reproductive performances were comparable with average performance figures of the New Zealand sheep farming industry.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Published NZ data</th>
<th>Model output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lambs tailed per lambing ewe</td>
<td>1.32</td>
<td>1.31</td>
</tr>
<tr>
<td>Percent of lambs born slaughtered for meat by December</td>
<td>21%</td>
<td>20%</td>
</tr>
<tr>
<td>Lambs slaughtered for meat per lambing ewe</td>
<td>1.01</td>
<td>0.92</td>
</tr>
</tbody>
</table>

The next step was to add MAP infection to the sheep model. Two infection pathways were considered, a fast ‘progressor track’ and a slow ‘non-progressor track’. Model structure and key parameters for the progression of infection towards clinical disease are shown in Figure 4.

![Figure 4: Structuring MAP infection pathways.](image)
The focus of the literature review was the age and dose dependent rate of infection ($\lambda$), the rate of cure from infection ($1-\gamma$), the proportion of infected sheep in different age groups that progressed to ‘low shedding (paucibacillary), ‘high shedding’ (multibacillary), and eventually clinical disease in each of the ‘progressor track’ ($\gamma$) and the ‘non-progressor track’, the time of staying in a low shedding state before progressing to high shedding and clinical disease in the ‘progressor track’ ($\delta$) and in the ‘non-progressor track’ ($\gamma$). In addition, the tissue load and the amount of shedding was of interest as this had a strong impact on the environmental contamination and consequently on disease dynamics. Associated with the severity of PTB specific histological lesions based on the system of Perez et al. (1996), the degree of mycobacterial colonization of the tissues allows the differentiation between paucibacillary lesions presenting no or few acid fast bacilli (AFB), or multibacillary lesions presenting abundance of acid fast bacilli (AFB) mainly located within macrophages (Clarke and Little 1996). Severe type of lesions (type 3) are characterised as multi-focal to diffuse and can be differentiated as paucibacillary (type 3a and 3c) or multibacillary lesions (3b). A meta-analysis of seven studies indicated that progression of infection to disease was highly likely when the dose at infection was greater than $8^{10}$ MAP (Figure 5). A similar analysis was done for the effect of age.

Model outputs of rates of infection, shedding and mortality were comparable to published data from Australia (Reddacliff et al. 2006, Morris et al. 2006). However, table 2 shows that ewe mortality rates of the model were somewhat higher than those shown by Morris et al. (2006) which may be attributable to a possibly slightly higher rate of progression to clinical disease of reported challenge studies (to which the model was adapted) than observable under natural challenge conditions. Moreover, published NZ survey data relied on farmer observed PTB specific ewe death rates which may have been underestimated. The truth may be somewhere between 1% and 1.8% annual OJD mortality. Model predicted prevalence was well within the large observed range.

![Figure 5: Tissue burden of MAP (in logCFU) over time depending on the dose of infection.](image)

Table 2: Comparison of model outputs of infection, shedding and mortality with published studies.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Published NZ data (Morris et al. 2006)</th>
<th>Model output</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence infected</td>
<td>??</td>
<td>70-80%</td>
</tr>
<tr>
<td>Prevalence of shedding</td>
<td>2-26%</td>
<td>6-7%</td>
</tr>
<tr>
<td>Annual OJD mortality (all ages)</td>
<td>2.9%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Annual OJD mortality (MA ewes)</td>
<td>1%</td>
<td>1.8%</td>
</tr>
</tbody>
</table>
3.2 Milestone 5.3.10 – Mixed species sheep-cattle model developed and presented

**Model development:** The development of a 2-host model of PTB was motivated by the fact that the majority of dry stock farms are running both sheep and beef cattle co-jointly on the same property. Evidence of MAP across species was indicated by molecular strain typing data revealing that sheep and beef cattle often share the same MAP strain. The first objective relevant to this milestone was therefore to develop a two-host (sheep and beef cattle) model of infection dynamics under different co-grazing (CG) regimes.

The sheep component is based on the work by Marquetoux et al. (2012) and was described above. This and a cattle model adapted from the literature were the basis for developing and evaluating a two-host model for ovine and bovine PTB. The mixed species model is described in detail in the PhD thesis of Verdugo (2013). The structure is shown in Figure 6. Sheep and cattle are jointly grazed, either on the same paddock for about 3 months during lambing and calving (July – October) or on separate pasture blocks, either in total isolation or by rotational, i.e. alternate grazing of paddocks one species after the other. Using this approach, grazing management could be varied to evaluate its impact on prevalence and clinical PTB over time. Available survey data about infection prevalence and clinical incidence in sheep flocks and beef cattle herds were used to calibrate the model.

The beef component was adapted from the model developed by Mitchell et al. (2008) for MAP transmission in dairy cattle. The adapted version considered the typical age structure and grazing management of beef in New Zealand, and included two possible progression tracks (transient shedding or latent) for newly infected animals. Beef were divided into four age categories: calves (0-6 months, subscript 1), weaners (6-12 months, subscript 2), heifers (12-24 months, subscript 3), and adult cows (>24 months, subscript 4). Even though rare occurrences of infection in adult cows has been observed (Mitchell et al., 2012), it was assumed that animals were fully resistant to infection after 12 months of age (Windsor and Whittington, 2010). Therefore, there were two susceptible bovine states (bS1 & bS₂) and two resistant bovine states (bR3 & bR₄) (Figure 6). Susceptible calves (bS1) could become infected at probability λ₃₁, and susceptible weaners at a probability λ₃₂ (Windsor and Whittington, 2010; Mitchell et al., 2012). Additionally, calves born from an infected dam were at risk of vertical/pseudo-vertical transmission with probability ρ₃. A newly infected animal could become a transient shedder (bTr₁ & bTr₂) with probability χ₃, or enter directly to a latent and slow-progression compartment (bLs₁ & bLs₂), with probability 1-χ₃ (McDonald et al., 1999; Stewart et al.,...
Transient animals stopped shedding and moved to a latent stage ($bL_1$ & $bL_2$) at rates $\delta_{b1}$ and $\delta_{b2}$. Finally, latent ($bL_4$) or latent-slow progressing cows ($bLS_4$) started to shed during adulthood (>24 months) at rates $\delta_{b3}$ and $\delta_{b4}$ respectively, where $\delta_{b3} > \delta_{b4}$. Infectious ($Y$) cows were first in a low shedding (ls) compartment ($bYls_4$) and then progressed to a high shedding (hs) state ($bYhs_4$) at rate $\delta_{b5}$. Animals in age categories 1-4 were dying of natural causes with probability $\mu_{b1-4}$ and high shedding animals additionally died of clinical disease at rate $\mu_{bc}$. Adult animals were culled at rate $\tau_b$ for normal management purposes.

The sheep model simulated the introduction and maintenance of MAP in a pastoral sheep flock under seasonal farming conditions in New Zealand. To make it comparable to the beef component, the seasonal pattern in the sheep flock demographics was omitted and age-specific characteristics of MAP infection dynamics were retained. Four age categories were considered: lambs (0-3 months, subscript 1), hoggets (3-12 months, subscript 2), two-tooth (12-24 months, subscript 3), and mixed age ewes (>24 months, subscript 4). All age categories were equally susceptible to infection, but rates of subsequent progression to disease versus recovery varied with the age at infection (Reddacliff et al., 2004; Dennis et al., 2011; Delgado et al., 2012; McGregor et al., 2012).

The environmental component (Env) holds MAP on pasture shed by infectious livestock for the time of survival, exposing susceptible sheep or beef to infection. Env was partitioned into 8-10 paddocks, depending on whether beef and sheep were managed in isolation, by co-grazing (CG) or by rotational grazing (RG). Animals were allocated to a paddock depending on species and age class.

**Model outputs:** In beef, the single species system levelled to an equilibrium infection prevalence of 13.1% with an annual clinical PTB incidence of 0.5%. At this endemic state, there were 17.7% susceptible, 69.1% resistant, 0.1% transient, 8.8% latent, 4.0% low shedding, and 0.2% high shedding animals. The equilibrium infection prevalence for the default single species situation of sheep was 19.9% with an annual clinical PTB incidence of 1.7%, and a population distribution of 79.8% susceptible, 5.9% paucibacillary (progressor), 3.3% paucibacillary (non-progressor), 10.2% resistant, and 0.8% multibacillary animals. When both species were infected on mixed-species farms and co-grazed for 3 months per year, infection prevalence in beef increased from 13.1 to 20.7%, and in sheep from 19.9 to 26.0%. When a herd or flock was initially naïve, the model predicted that it may last about 15-20 years for prevalence to increase from 0% to 10% in beef cattle, but only about 10-12 years for sheep. Prevalence increased further for several decades before equilibrating to a constant endemic level. Data from field surveys of JDRC baseline studies and model predictions of prevalence and clinical PTB incidence were reasonably similar considering that baseline incidence data based on questionnaire data, hence subject to recall and observation bias (Table 3).

### Table 3: Comparison of prevalence and incidence of baseline survey data with model outputs.

<table>
<thead>
<tr>
<th>Farm types</th>
<th>Observed Prevalence (%)</th>
<th>Observed Incidence (%)</th>
<th>Simulated Prevalence (%)</th>
<th>Simulated Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep only</td>
<td>20</td>
<td>0.16</td>
<td>19.9</td>
<td>1.7</td>
</tr>
<tr>
<td>Beef only</td>
<td>13</td>
<td>0.04</td>
<td>13.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Sheep (S&amp;B)</td>
<td>21</td>
<td>NA</td>
<td>26.0</td>
<td>2.3</td>
</tr>
<tr>
<td>Beef (S&amp;B)</td>
<td>17</td>
<td>NA</td>
<td>20.7</td>
<td>0.7</td>
</tr>
</tbody>
</table>

NA = Not available

Transmission of MAP across species occurred when naïve beef or sheep were concurrently co-grazed with their infected counterpart for periods of 2 to 6 months per year. However, the effect was not the same for both species: transmission was faster from infected beef to naïve sheep than vice-versa. But it could take up to 20 years for naïve beef cattle and up to 10 years for naïve sheep to reach 10% prevalence when sharing pasture with the other infected species (Figure 7).
3.3 Milestone 5.3.11: Cost-effectiveness of intervention scenarios evaluated and presented for single species farms

3.3.1 Deer

Based on model outputs, early detection of young deer in a high-shedding state was the most effective means of controlling PTB among the tested scenarios (Figure 8). Since early detection may not be associated with high cost (e.g. extra labour time), increased herd monitoring is likely to be cost effective. On the contrary, testing and removal by ELISA did not reduce prevalence as infection of additional susceptible replacement fawns entering the herd increased prevalence to the same extent as the culling of test positive shedding and non-shedding (false positive) deer decreased it. Hence T&C could neither be efficient nor cost effective.

3.3.2 Sheep

According to 2012 prices, the annual loss due to PTB was estimated to be NZ$3.2 per ewe (2013 prices: NZ$2.6). At a population of 38m adult sheep and assuming 75% were on OJD-infected farms (Verdugo 2013), the total annual loss at national level would range NZ$75-92m. The model suggested that 93.5% of the total annual loss was due to mortality, 82% due to the OJD related death of adult ewes plus 11.5% of lambs, growers and hoggets. The remaining 6.5% were attributable to lower growth of replacement hoggets (0.5%) and poor reproductive performance (sub-fertility, 6%).

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Vaccination assumed that lambs would be vaccinated at weaning (3m of age) and that only vaccinated lambs would be kept for replacement. Selection for replacement is usually done at tailing/docking at a lower age (<3m). As Figure 9 shows, annual clinical incidence (and prevalence) would start to effectively decrease at about 2 years after starting vaccination and reduce to zero at about 9-10 years. This suggests that farmers need to maintain vaccination for an extended period before they would realise production benefits. A second question that could be evaluated is the effect of stopping vaccination after 10 or more years.

The cost effectiveness of vaccination strongly depended on the level of mortality in the flock. The model suggested that positive returns over investment were achieved if PTB caused 1.8% mortality whereas 0.75% mortality would not render vaccination as cost-effective (Figure 10).

A second control strategy evaluated by the model was test&cull (TC). This was based on testing ewes in low body condition with an ELISA with near 80% sensitivity and 99% specificity. Such ewes would be in a pre-clinical or early clinical stage of OJD. According to the model, there were about 5% mixed age ewes in low-shedding (paucibacillary) and 0.9% in a high-shedding (multibacillary) stage of OJD progression at the time of culling. Only few ewes would be expected in a state of low body condition and thus drafted for testing. Consequently, TC was not an effective strategy for controlling OJD and not cost effective. More strategies can be evaluated such as the length of time that vaccination would have to be continued to achieve a sustained low or zero prevalence.

Model parameters and scenarios were and will be continuously reviewed and updated. A significant impact on model updates are expected to arise from the current OJD economic study in 20 sheep flocks. Results of this study are expected towards mid-2015.

3.3.3 Sheep & Beef

The second objective the 2-host sheep and beef model was to evaluate the effect of various disease control measures on prevalence. Three control scenarios were evaluated: (i) Grazing of a naïve species on MAP-contaminated pasture after spelling pasture from grazing for several months; (ii) Test & cull (T&C) of animals, alone or in combination with (iii) increased ‘farmer surveillance’ for early identification and removal of pre-clinical animals (high shedders), and (iv) combining options (ii) and (iii). In a situation where both species were infected, option (v) grazing the two species in isolation was evaluated.
(i) **Extending pasture spelling periods**: Rotational grazing infected naïve sheep when they were grazing pasture that was previously contaminated by infected beef cattle and spelled for 6 months. However, it took about 50 years before flock infection reached a prevalence of 10%. In naïve beef cattle, a similar rotational grazing on MAP contaminated pasture with spelling times of 6 months or longer almost prevented PTB to reach noteworthy infection prevalence. Increasing the spelling period from 9 to 15 months reduced pasture contamination with MAP by up to 99%. Even though infection of naïve animals was still possible after such long spelling times, the resulting infection prevalence remained <1% for at least 25 years, thus transmission was effectively prevented. However, such long spelling periods may not be realistic under practical conditions of most farms. Thus, pasture spelling did not appear to be a recommendable control option.

(ii) **Test & cull**: Albeit being the most costly control method, annual T&C using a serum-ELISA decreased infection prevalence of beef cattle from 20% to an equilibrium of 4% after 25 years. Initially, a fast reduction to 10% was achieved within 6 years (Figure 11A). The effect was only slightly more profound when applied to both sheep and beef cattle (Figure 11B). At such prevalence, a flair-up must be expected to occur if T&C was discontinued (a scenario still to be simulated). Conversely, T&C did not reduce prevalence markedly in sheep when applied to sheep only: prevalence decreased from 25% to 17% within about 25 years (Figure 11C). However, when T&C was applied to both species, the effect in sheep was approximately doubled (Figure 11D)
(iii) **Farmer surveillance:** identifying and removing clinically diseased PTB animals by increased observation (and thereby removing shedders earlier) had marked effects on prevalence in sheep, but only modest effects in beef cattle. The effect in beef cattle appeared to be substantially greater when this increased surveillance was applied to both species simultaneously (Figure 11).

(iv) **Combining T&C with surveillance:** When T&C was combined with increased farmer surveillance, the extra reduction in prevalence of beef cattle was relatively marginal. On the contrary, adding surveillance to T&C in sheep had a much larger effect than T&C alone. In fact, modelling suggested that surveillance alone accounted most of the total effect of control. Hence, quite clearly, T&C was most effective in beef cattle whereas farmer surveillance was effective in sheep. Thus, whole flock T&C cannot be a cost effective control strategy for sheep whereas surveillance potentially provides economic incentives for control. From a cost-benefit perspective, surveillance is certainly a low cost option, hence probably the most attractive control method (still to be simulated). It is particularly
effective in sheep, and to a lesser extent in beef cattle. Applying surveillance to beef cattle and sheep simultaneously increased its effectiveness substantially.

**(v) Species isolation:** grazing different paddocks without overlap at any time could not control PTB prevalence in any species when both were initially infected. However, in combination with increased farmer surveillance, species isolation reduced the prevalence rapidly in sheep but only quite slowly in beef. However, this combination was the most effective intervention for both species. Its cost-effectiveness is subject to the additional consideration of cost items, revenues and discounting of monetary values over time.

**References**


