Options For Use Of A Vaccine Against Tuberculosis In Domestic And Wild Animals In New Zealand

P.G. Livingstone

Introduction

Bovine tuberculosis (Tb) caused by *Mycobacterium bovis* is endemic in wild animal populations in 26 defined areas of New Zealand. These areas, where infected wild animal species act as vectors of tuberculosis for cattle and farmed deer, are known as Tb Vector Risk Areas (VRAs)[1]. While it is possible to eradicate infection from infected cattle and deer herds in VRAs through a test and slaughter regime, herds become reinfected unless vector populations are also controlled and maintained thereafter at low densities. Vector control has resulted in tuberculosis being eradicated from cattle, farmed deer and possum populations in 4 small (5 - 10,000 ha) areas since 1993.

Vector control has also been responsible for a marked reduction in the number of Tb-infected cattle herds, from a peak of 1,527 (2.6%) in October 1994, to 1,108 (1.7%) at the end of May 1997. The number of infected deer herds has also fallen, from a peak of 277 (5%) in July 1991, to 128 (2.3%) at the end of May 1997. Nevertheless, the percentage of infected cattle herds is still high relative to that of our trading partners which all have less than 0.2% herds infected. New Zealand's overarching concern with tuberculosis in domestic livestock is the potential threat the disease poses to our ability to trade with prime markets (Livingstone, 1993).

In spite of the success of vector control in reducing the number of infected herds, the size and number of VRAs has continued to increase, particularly in the extensive, rabbit prone areas of the South Island. Vector control is expensive, costing $18.3 million in 1996/97 and an estimated $27 million in 1997/98. While research and technical improvements in possum control have improved the effectiveness of control operations, there is a lack of knowledge and techniques available for cost-effective control of other potential vector species (feral deer, pigs and ferrets).

In the early 1990s the expanding size and number of VRAs and the consequent threat the disease poses to our primary industries stimulated an increase in funds for research. A

[1] A Tb Vector Risk Area is defined as a geographical area where either epidemiological information from infected cattle and deer herds indicates a wild animal source of infection , or tuberculosis has been identified in wild animals which are considered a source of infection for livestock

National Science Strategy Committee (NSSC) for control of possums and bovine tuberculosis was established in 1991 to "enhance the coordination of all research programmes on possum/bovine tuberculosis control" (Wright, 1993). A component of NSSC's research strategy is the development of vaccines that will either protect domestic livestock or reduce the ability of wild animals to spread tuberculosis both amongst themselves and to domestic livestock.

From very modest beginnings in 1990, vaccine research has progressed rapidly. New Zealand now has a large group of researchers who are recognised internationally for their innovative research work on tuberculosis immunology and vaccine development. The NSSC is intending to review vaccine research to ensure it is coordinated, integrated and directed towards a common goal. Similarly, the Animal Health Board has to assess the likely cost-effectiveness of using vaccines to reduce herd Tb incidence. The objective of this paper therefore is to assess the constraints and potential uses for a vaccine against bovine tuberculosis in New Zealand.

The Rôle Of Vaccination

The objective of vaccine research is the development of an efficacious vaccine and vaccination strategy that will protect cattle and farmed deer from infection with *Mycobacterium bovis*. There are two strategic options for the employment of vaccines in Tb control. The first option is the direct vaccination of livestock to provide protection from *M. bovis* infection. The second is vaccination of wild animal vector populations to reduce the exposure of cattle and farmed deer to the main source of infection. Currently both of these options are being pursued. Future vaccine research, and the development of vaccination tactics depend on which strategic option, or combination of options, is chosen. Factors likely to influence future research direction and strategy implementation include:

- vaccine efficacy under field conditions;
- species targeted for vaccination;
- costs associated with achieving Tb control or eradication objectives through vaccination, compared to existing methods;
- effects of a vaccine on the interpretation of diagnostic tests;
- assessed national and international reaction to:
  - * current vector control methods;
  - * herd Tb prevalence levels;
  - * vaccine type and target species.

Vaccination Of Cattle And Farmed Deer

The aim of vaccinating cattle and farmed deer is to protect them from infection with *M. bovis*, without producing a Delayed Hypersensitivity Reaction to intradermal tuberculin

tests. Cycling of infection within cattle and deer herds is uncommon in New Zealand (estimated by the author at 3% and 7% of infected herds respectively in 1996/97). Because cycling of infection within herds is so uncommon and generally responds rapidly to a test and slaughter programme (Tweddle & Livingstone, 1994), vaccination of all herds in New Zealand to prevent such occurrences would not be an economical option.

However, more than 85% of infected cattle and deer herds are located in the 26 VRAs, where vectors of tuberculosis, such as possums, feral deer, ferrets and possibly feral pigs, act as sources of infection for domestic and wild animals (Tweddle & Livingstone, 1994). Therefore cattle and farmed deer in the VRAs are the obvious candidates to be vaccinated, given their potential exposure to tuberculous wild animal vectors. To be effective under these conditions, the vaccine must:

- protect >95% of challenged cattle from becoming infected (Livingstone & Davidson, 1993);
- provide life long protection;
- cost less than $1.00/animal;
- not stimulate a Delayed Hypersensitivity Reaction to intradermal tuberculin tests.

Vaccine efficacy

The only vaccine likely to be approved internationally for use in cattle and deer within the near future is the vaccine derived from the bacillus of Calmette-Guerin (BCG) (OIE, 1996). Even though it has been used in 2 - 3 billion humans, its efficacy and safety will need to be proven before products derived from vaccinated animals will be accepted internationally. BCG is the 'gold standard' vaccine and is currently being trialed in cattle, deer and possums in New Zealand. Meanwhile, a number of other vaccine types are being investigated for use in domestic livestock and wild animal vector populations (Buddle, 1997), but gaining international acceptance of their efficacy and safety could take 10 years.

Research has identified that cattle vaccinated subcutaneously with a single low dose (5 x 10^4 cfu) of BCG became infected following intratracheal challenge, whereas aerosol vaccination was successful in preventing the development of lung lesions (Buddle et al., 1995). The Tb Research Group at Otago University identified that two subcutaneous low doses of BCG vaccine induced an 80 - 90 % protection against pathological disease in farmed deer following intratonsil challenge, compared to 60% achieved in response to single dose vaccinations (Hook et al., 1995). Further work suggests that three doses are superior to double doses (Deer Research Laboratory, 1996)

A number of conditions such as stress and prior exposure to saprophytic mycobacteria can affect the efficacy of the vaccine. Conditions that induce a chronic stress response causing corticosteroid hormone levels to rise significantly reduced the efficacy of BCG in protecting animals against challenge with *M. bovis*. Similarly, deer treated with dexamethasone 3 weeks before being vaccinated with BCG had a significantly reduced

protection against disease than deer that had not received dexamethasone (Thompson et al., 1995).

It was also found that the efficacy of BCG vaccine can be influenced by prior 'imprinting' of the immune responses by saprophytic mycobacteria. It is hypothesised that if the inappropriate *Th-2 type* immune response is generated by this prior exposure, then subsequent vaccination with BCG may not overcome the imprinting, and will fail to protect vaccinated animals (Buchan et al., 1995). There is some evidence that genotype can influence the way that macrophages are able to control the replication of *M. bovis* (Templeton & Adams, 1995; Mackintosh, 1997). Therefore if cattle and deer that are less resistant to *M. bovis* can be identified, these animals, as well as animals under stress, could be vaccinated with a recombinant BCG vaccine containing a cytokine gene which stimulates the appropriate *Th-1 type* immunological pathway, leading to a protective response.

Unless our trading partners can be convinced that the vaccine used will prevent infection in all vaccinated cattle and farmed deer, diagnostic testing will still be required. Attainment of this level of efficacy is highly improbable. Therefore the vaccine selected must not sensitise animals to intradermal tests. Data from current research on vaccination of cattle and deer with BCG indicate that some animals are still sensitised to bovine PPD for up to 18 months after vaccination (OIE, 1996). Recent studies though show that intratracheal vaccination with BCG, or use of a sub-unit vaccine, induced negligible skin test response whilst providing protection against virulent *M. bovis* (Buddle et al., 1996).

In the VRAs, cattle and deer will continue to be exposed to, and therefore challenged by, infected wild animals. Thus there is an on-going opportunity for the size of the challenge to overcome the immune response, resulting in Tb lesions, so there will be a continuing need for diagnostic testing. An ideal vaccine would prevent invasion at the mucosal surface, such that no immune response would follow challenge. If instead, the vaccination response is to minimise multiplication of *M. bovis* such that infection becomes 'dormant', these animals will almost certainly react to intradermal tuberculin tests, but will have 'no visible lesions' on slaughter. Therefore a cheap test that is able to differentiate between vaccinated animals that have uncontrolled tuberculosis and animals that either have an increased sensitivity following challenge, or have dormant infection, will be required before farmers will allow cattle to be vaccinated as part of a national Tb control programme in VRAs.

Regardless of efficacy results obtained under trial conditions, efficacy under field conditions is critical. A field trial has yet to be undertaken in New Zealand to establish efficacy under natural challenge and to determine the length of time vaccinated animals will be protected from infection. The critical aspect of a field trial will be to include sufficient vaccinated and unvaccinated animals to ensure a statistically significant result is achieved following natural challenge. Designing and implementing such a trial will be challenging, time consuming and expensive. Therefore it behoves researchers to ensure that the vaccine trialed is the one that best meets the conditions listed previously.

Implications for vector control

If all cattle and deer within VRAs could effectively be vaccinated there are two possible scenarios for future vector control programmes. The first is that the vaccine used is sufficiently efficacious to withstand any challenge from Tb wild animal vectors. Under this scenario, vector control within the VRA could be stopped, though control of vectors within a buffer zone surrounding the VRA would continue in order to minimise their outward spread. The second scenario is that if the vaccine used is not sufficiently efficacious, then without concomitant vector control, the infected wild animal population will continue to challenge both vaccinates and the buffer zone.

Comparison of no vaccination with various vaccination scenarios (assuming 95% vaccine efficacy) in VRAs, without vector control, showed that vaccination was only cost-effective when vaccinated cattle mount a Delayed Hypersensitivity Reaction to tuberculin for a short time after contact with *M. bovis*, or a relatively cheap *in-vitro* differential diagnostic test is available (Livingstone & Davidson, 1993). However, all vaccination scenarios significantly reduced the number of tuberculous cattle (and therefore the number of false negative cattle) when compared to unvaccinated cattle.

Vaccination may reduce herd Tb prevalence levels in VRAs faster than is being achieved through current vector control techniques. It may also assist in preventing reinfection of herds if wild animal control was either no longer publicly accepted or was too expensive. However, if no wild animal control was undertaken, the end result would be spread of vectors and enlarged VRAs, requiring increasingly more herds to be vaccinated. Therefore the main priority is containment of infection within VRAs.

Vaccination Of Wild Animal Species

Possums, ferrets and feral deer are accepted as vectors of Tb for cattle and farmed deer (Luton et al., 1995; Morris, 1995; Livingstone, 1996; Ryan et al., 1996), and are the animal species within which the disease is cycling either directly or indirectly (Hickling, 1995). Sustained vector control is targeted at reducing the vector population density below the threshold for transmission of Tb, with the objective of eradicating the disease where this is technically feasible. A possible alternative that could be used to break or assist in breaking the disease cycle, is to vaccinate the susceptible wild animal population against Tb, in a similar manner to the way that vaccination of foxes against rabies in Europe has reportedly stopped the spread of this disease (Morris et al., 1993). This success is currently being questioned though (Barlow, 1996).

Vaccine efficacy

For wild animals, vaccine efficacy could be lower than for domestic livestock, as it only needs to prevent excretion of *M. bovis* (Morris et al., 1993). However, it is currently unknown whether this level of efficacy can be achieved in possum populations. Results from pen and cage studies indicate that possums vaccinated subcutaneously, intratracheally or intraduodenally with BCG have smaller lesions and live longer when

challenged with *M. bovis*, compared to both orally vaccinated and unvaccinated animals (Buddle et al., 1995; Buddle et al., 1996; Morris pers.comm.). Nevertheless, 'successfully' vaccinated possums still had pathological disease and therefore may in the end be just as potent a source of infection for domestic and wild animals as non-vaccinates. Wild animal populations will also be subject to the same vaccine efficacy problems as identified for cattle and deer, ie. prior 'imprinting', stress and genetically variable immune response.

In addition, a number of unknowns will need to be resolved before vaccination of wild animals can proceed, including:

- effectiveness of the immune response in preventing animal to animal spread of tuberculosis;
- the length of time that immunity lasts after vaccination;
- effect on the immune response when free-living wild animals are exposed to multiple doses of vaccine either at a point in time or over a short period of time (days);
- effect on immune response and resistance to Tb if the booster dose is not received at the right period of time after the initial dose;
- the ability to attract a sufficient proportion of the targeted population to a vaccine dispensing unit or bait in order to break the disease transmission cycle more cost-effectively than current vector control techniques.
- presentation of the vaccine such that it retains its viability and stimulates an effective immune response when dispensed as an aerosol or incorporated in a bait.

Application of vaccine to wild animal populations

Because of the expense associated with trialing a vaccine in wild animal populations, a number of scenarios have been compared through the use of mathematical or computer simulation models. These models have indicated that so called "culling" or reducing the density of the possum population to low levels is the preferred strategy to prevent Tb from spreading to a disease free possum population. However, depending upon the model, vaccination may be just as effective at removing Tb from the population as vector control (Roberts, 1995; Kalmakoff et al., 1995), or less effective (Barlow, 1995).

Barlow & Kean (1995), indicate that vaccination of possums in buffer zones offers the best method of control when populations are near carrying capacity. In this situation, dispersing juveniles will not be able to compete with the resident population for food and den sites, and will therefore suffer a higher mortality. However, this scenario requires the population in a large area to have been vaccinated for a long period of time. Another scenario is to reduce the possum population to a low density in a broad area and vaccinate juveniles moving into the bush/pasture margin zone where the vaccine would be deployed. As a consequence the possum population along the bush/pasture margin (where it is usually most dense) will be vaccinated. Theoretically this population would act as an immune buffer preventing establishment of foci of infected possums along the bush/pasture margin and would thus greatly reduce the risk of cattle or farmed deer becoming infected when grazing in the vicinity.

So far, research into vaccines for possums and feral deer is at an early stage, with the deer work looking most promising.

Implications of vaccinating wild animals

For a Tb vaccine to work on a susceptible free-living wild animal population, animals will have to be attracted to vaccine deployed either via an aerosol or in a bait. However, field deployment of a vaccine would also provide an opportunity for cattle, farmed deer and sheep to gain access to the vaccine, with potential impacts on diagnostic tests and international market acceptance of livestock products. Impacts on non-target native animals will also need to be investigated. Further, use of a vaccine could impact on exporting of game from these areas.

Once a policy of vaccinating wild animals has been adopted, it will need to be pursued until the disease cycle involving the wild animal population has been broken. This will take up to 10 years. Depending on the control strategy adopted, the cost of vaccination may be offset by reduced vector control. If vaccination replaced vector control, possums and other wild animal populations will increase, thereby threatening conservation values. Therefore this strategy is likely to be opposed by conservationists. Indeed sceptics would say, if the targeted wild animals are ingesting a bait or inhaling from an aerosol, they should be poisoned rather than vaccinated. Therefore the additional cost of maintaining conservation values would have to be assessed in any comparative Benefit/Cost analysis.

Vaccination of wild animal populations is unlikely to raise international controversy, provided domestic livestock do not become exposed to the vaccine. It also provides an opportunity to use more efficacious vaccines than BCG earlier than they could be used in domestic livestock.

Incentives for the development of wild animal vaccination

Under present circumstances, the benefits of vaccinating wild animals against tuberculosis compared with current vector control technology appears marginal. However, any compromises in the effectiveness of current technology could shift the balance in favour of a vaccination strategy. For example, the use of 1080 poison could be restricted by national or international pressure, vector populations could develop aversions to toxic baits, or the costs of control could escalate. Furthermore, the development of a vaccine strategy for wild animals would provide another tool which could be used in a package of integrated control measures.

Conclusions

The acceptance of a vaccination policy for cattle and farmed deer in VRAs will be predicated on winning international acceptance for the use of a vaccine of high efficacy (>95%), which is more cost-effective than a policy of non-vaccination. The vaccine must not cause prolonged sensitisation to intradermal tuberculin tests, and would ideally prevent invasion of the mucosal surfaces. If it is allergenic, then a cost-effective test needs to be available to differentiate tuberculous animals from non-tuberculous test positives.

Genotypes that have been identified as less resistant to *M. bovis,* and cattle and deer that are under stress may have to be treated differently. To implement such a vaccination programme will require a technologically advanced vaccine and diagnostic technology, together with a targeted programme to ensure farmer cooperation to achieve success.

Further, any policy to implement a vaccination strategy, assuming a vaccine meeting our specifications was available, must be adopted well in advance of the imposition of any Tb-related trade barriers, because of the 2 - 3 year time lag before vaccination would bring about a reduction in number of infected herds.

The author considers that there is a low probability that a suitable vaccine will be available for use in cattle and farmed deer in New Zealand within the next 10 years. If a suitable vaccine was available its likely role would be to protect cattle and deer in VRAs which were not part of a vector control programme. Although it seems unlikely that there will be significant use of Tb vaccines in cattle and deer in New Zealand, it is important to note that New Zealand vaccine research may have implications for bovine Tb control in developing countries, where traditional test and slaughter programmes are unaffordable (OIE, 1996). This could also have human health benefits in these countries. There is, therefore, an argument for continuing current lines of research in light of potential applications areas; but this research should not be a cost to the New Zealand Tb control programme.

With regard to vaccination of wild animals, vaccination alone will not eradicate endemic tuberculosis. Instead, it potentially provides another management tool that can be integrated with vector control to assist in the containment and eradication of Tb from wild animal populations in VRAs. In this regard, consideration must be given to the need to vaccinate other wild animal vectors apart from possums.

It is recommended that New Zealand's vaccine research be directed towards a strategy of vaccinating wild rather than domestic animals.

Acknowledgements

The author wishes to thank Nick Hancox for his constructive editorial assistance, and Dr de Lisle and Professors Morris and Griffin, for the review that they jointly prepared for the AHB (de Lisle et al., 1996) which formed the basis of this paper.

References

Barlow, N.D (1995) Simple models for TB and possum control. In F Griffin & G de Lisle (Eds) *Tuberculosis in Wildlife and Domestic Animals* Otago Conference Series No. 3, Dunedin, pp 161 - 164.

Barlow, N.D. (1996): Modelling vaccination of possums *Vaccination as a means for control of bovine tuberculosis* Proceedings of a Workshop organised by the Possum and Bovine Tuberculosis Control National Science Strategy Committee, 27 - 28 November 1996, Wallaceville, The Royal Society of New Zealand, Wellington, pp 47 - 49

Barlow, N.D. & Kean, J.M (1995): Spatial models for tuberculosis in possums In F. Griffin & G de Lisle (Eds.) *Tuberculosis in Wildlife and Domestic Animals*. Otago Conference Series No. 3, Dunedin, pp 214 - 218

Buchan, G , Lochart, E , Slobbe, L., Chinn, N , Hook, S , Thompson, A & Griffin, J F.T. (1995) BCG Vaccination. Can it be improved? In F. Griffin & G. de Lisle (Eds.) *Tuberculosis in Wildlife and Domestic Animals* Otago Conference Series No 3, Dunedin, pp 116 - 120.

Buddle, B.M (1997) Advances in the development of more cost effective vaccines against bovine tuberculosis This Proceedings

Buddle, B M , Aldwell, F.E. & Wedlock, D.N. (1995) Vaccination of cattle and possums against bovine tuberculosis In F Griffin & G de Lisle (Eds) *Tuberculosis in Wildlife and Domestic Animals* Otago Conference Series No 3, Dunedin, pp 111 - 115.

Buddle, B M , Aldwell, F E., Wedlock, D.N. & de Lisle, G W (1996) Vaccination of cattle and possums against bovine tuberculosis. *Vaccination as a means for control of bovine tuberculosis* Proceedings of a Workshop organised by the Possum and Bovine Tuberculosis Control National Science Strategy Committee, 27 - 28 November 1996, Wallaceville, The Royal Society of New Zealand, Wellington, Addendum

Deer Research Laboratory, (1996) Vaccine Research *Vaccination as a means for control of bovine tuberculosis*: Proceedings of a Workshop organised by the Possum and Bovine Tuberculosis Control National Science Strategy Committee, 27 - 28 November 1996, Wallaceville, The Royal Society of New Zealand, Wellington, p 35.

de Lisle, G.W , Griffin, J F T & Morris, R S (1996) *Vaccination as a means for control of bovine tuberculosis* Proceedings of a Workshop organised by the Possum and Bovine Tuberculosis Control National Science Strategy Committee, 27 - 28 November 1996, Wallaceville, The Royal Society of New Zealand, Wellington, pp 99 - 112

Hickling, G. (1995): Wildlife reservoirs of bovine tuberculosis in New Zealand In F Griffin & G. de Lisle (Eds.) *Tuberculosis in Wildlife and Domestic Animals*. Otago Conference Series No 3, Dunedin, pp 276 - 279

Hook, S., Slobbe, L., Chinn, N., Griffin, F., Hesketh, J , Mackintosh, C & Buchan, G (1995) Measuring cytokine responses to vaccination with live and killed BCG. In F Griffin & G de Lisle (Eds) *Tuberculosis in Wildlife and Domestic Animals*. Otago Conference Series No 3, Dunedin, pp 128 - 130

Kalmakoff, J., Mackintosh, C., Griffin, J.F.T. (1995) A pseudovertical transmission model for the epidemiology of tuberculosis in New Zealand possums In F Griffin & G de Lisle (Eds) *Tuberculosis in Wildlife and Domestic Animals*. Otago Conference Series No. 3, Dunedin, pp 225 - 227

Livingstone, P.G. (1993) Production pests: what values need protection? *New Zealand Journal of Zoology* 20: 273-277

Livingstone, P.G. (1996): Overview of the ferret problem *Ferrets as vectors of tuberculosis and threats to conservation* Proceedings of a Workshop organised by the Possum and Bovine Tuberculosis Control National Science Strategy Committee, 27 - 28 March 1996, Lincoln, The Royal Society of New Zealand, Wellington, pp 2-6

Livingstone, P G. & Davidson, R M (1993): A discussion on the role of vaccination against tuberculosis. *Report on Workshop on "Vaccination as a means for control/eradication of bovine tuberculosis"*, Ministry of Research Science and Technology, Wellington, pp 19-33

Luton, I , Morris, R., Wilson, P. & Griffin, J.F.T. (1995) Natural Infection of red deer with tuberculosis In F. Griffin & G. de Lisle (Eds.) *Tuberculosis in Wildlife and Domestic Animals* Otago Conference Series No 3, Dunedin, pp 280 - 283

Mackintosh, C (1997): (This proceedings)

Morris, R S (1995): Epidemiological principles for tuberculosis control In F. Griffin & G. de Lisle (Eds) *Tuberculosis in Wildlife and Domestic Animals* Otago Conference Series No. 3, Dunedin, pp 210 - 213

Morris, R.S., Pfeiffer, D U & Jackson, R. (1993) Epidemiological Issues in the Development and Application of Animal Tuberculosis Vaccines. *Report on Workshop on "Vaccination as a means for control/eradication of bovine tuberculosis"*, Ministry of Research Science and Technology, Wellington, pp 14-18.

OIE, (1996) *Report of the meeting of an OIE ad hoc group on bovine tuberculosis control in developing countries*, Office International des Epizooties, Paris.

Roberts, M (1995): Tuberculosis control in possums· culling or vaccination? In F Griffin & G de Lisle (Eds) *Tuberculosis in Wildlife and Domestic Animals* Otago Conference Series No 3, Dunedin, pp 222 - 224.

Ryan, T.J., Pannett, G R & Adams, J.L. (1996) Possums and tuberculosis control in cattle and deer *Improving conventional control of possums* Proceedings of a Workshop organised by the Possum and Bovine Tuberculosis Control National Science Strategy Committee, 25 - 26 October 1995, Wellington, The Royal Society of New Zealand, Wellington, pp 7-10

Templeton, J. & Adams, G (1995): Genetics of natural resistance to tuberculosis In F Griffin & G de Lisle (Eds) *Tuberculosis in Wildlife and Domestic Animals*. Otago Conference Series No 3, Dunedin, pp 29 - 32

Thompson, A., Mackintosh, C. & Griffin, J.F.T. (1995) The effect of dexamethasone on the protective efficacy of *Mycobacterium bovis* BCG in deer. In F. Griffin & G. de Lisle (Eds.) *Tuberculosis in Wildlife and Domestic Animals*. Otago Conference Series No 3, Dunedin, pp 131 - 134

Tweddle, N.E & Livingstone, P G. (1994). Bovine tuberculosis control and eradication programmes in Australia and New Zealand *Veterinary Microbiology* 40. 23-39

Wright, D E (1993): *Report from the Possum/Bovine Tuberculosis Control National Science Strategy Committee*, Ministry of Research Science and Technology, Wellington, p 3