Final report

Probio-TICK – Tick control Nature's way

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Executive summary

Background

Ectoparasites (ticks and buffalo fly) of cattle are estimated to cause major economic loss exceeding $250M p.a. to profitable beef production in northern Australia. Management of these pests relies on the dual approach of host genetics and chemicals. The former is challenging in view of market demand for better eating quality, and the latter faces the loss of efficacy due to acaricide resistance and the ever-present risk of residues in edible tissues. Reduction of cattle tick and buffalo fly from high to low infestation has the potential return up to $147M/pa to the cattle industry and related businesses. This demonstrates that full control is not required in order to deliver financial benefits to producers. In addition to these costs, the cost of compliance and maintaining tick quarantine barriers is high.

One approach to circumvent both these shortcomings is to exploit endemic, biologically active microbes which can supplement the host animal's ectomicrobiome and work to protect the animal against ectoparasite infestation.

Probio-TICK is a novel concept that applies the well-accepted health benefits of human "inner-health" probiotics to the "outer-health" of cattle hides by boosting the animal's innate resistance to pest invasion. Probio-TICK contains a community of beneficial microbes with known biological activity against ectoparasites which is applied to the hide of cattle. Proof-of-concept field trials conducted between 2017 and 2020 consistently demonstrated that Probio-TICK reduces tick numbers in cattle facing natural challenge thus opening a way to a natural, chemical-free approach to tick control.

Objectives

The objective of 'Probio-TICK –Tick control Nature's way' was to develop the scientific and commercial credentials of Probio-TICK as an aid for control of cattle tick. This covered development and manufacture of the preferred formulation, establishing the regulatory approval pathway with APVMA, conducting field investigation to provide data on efficacy and safety, and consulting with stakeholders regarding the commercial and practical aspects of the manufacture and field use of Probio-TICK.

Methodology

Microbial strains endemic to northern Australia used in proof-of-concept field trials were ranked on the basis of biological activity and growth characteristics and three were selected for the active pharmaceutical ingredient (API). The preferred formulation of the finished product (FP) was established at MST's laboratory based on rating of scientific, logistic and end-use parameters. FP was manufactured at a GMP-licensed manufacturer for stability studies and field trials. A protocol for a dose-determination field trial was developed and the trial undertaken to confirm the appropriate dose of the preferred formulation.

Results/key findings

Probio-TICK was developed for manufacture under GMP conditions as a powder for reconstitution with water. Stability studies are in progress. The dose determination field trial comparing 0.5x, 1x and 2x target dose demonstrated statistically significant reductions in tick burden of between 50 and 90% when comparing treatment groups with the control group, although no dose-response was seen. The effects of Probio-TICK persisted for approximately 2 – 3 weeks after application of the last

dose of IVP (investigational veterinary product). No adverse effects were seen on cattle; in particular, there were no adverse signs around the application sites.

Benefits to industry

The project has reinforced the potential benefits of the Probio-TICK microbes to aid in control of ticks in Northern Australia. The opportunity for organic control is attractive in markets where chemical use is banned.

Unfortunately, the regulatory environment is not flexible enough at this time to consider biological products outside the guidelines designed for use of chemicals necessitating a different approach to the development of Probio-TICK.

Future research and recommendations

MST intends to continue investigations into the commercial potential for Probio-TICK.

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1. Background

1.1 Cattle Tick in Northern Australia

Cattle tick is the costliest disease of cattle in northern Australia. As well as being parasitic on cattle skin, cattle ticks spread blood-borne diseases, lower the value of the livestock, and increase the costs of production via expenditure on agrochemicals and labour in northern Australia's successful broadacre properties. In the long term, the failure to control parasites limits the introduction of genetic traits for improved quality from ectoparasite-susceptible European breeds.

Tick control has historically relied on chemical acaricides which have the drawback of leaving meat residues and selecting for chemical resistances in ticks. Resistance limits pesticide efficacy year by year.

In 2015, the cost of ectoparasites, primarily cattle tick and buffalo fly, was calculated to be $260M/pa, an average of $60.47 per animal (see MLA report B.AHE.0010). Reduction of cattle tick and buffalo fly from high to low infestation has the potential return up to $147M/pa to the cattle industry and related businesses. This demonstrates that full control is not required in order to deliver financial benefits to producers. In addition to these costs, the cost of compliance and maintaining tick quarantine barriers is high. This includes thousands of kilometres of maintained double fences, aerial surveillance of tick lines, tick dipping stations and yarding facilities adjacent to many major roads in northern Australia. These treatment and prevention options have not changed significantly for many years.

Many decades ago, the introduction of *Bos indicus* crossbreeds provided the first landmark evidence of a natural solution against ectoparasite infection. Today, we understand this genetically-based resistance owes its protection partially to an immune response against larval ticks but also relates to characteristic skin biology and structure in indicine cattle (Jonsson NN et al (2014) Parasite Immunology DOI:10.1111/pim.12140). The concept of Probio-TICK is to develop an alternative to chemical acaracides by applying a collection of natural microbes to the hide of cattle in order to provide a shield against ticks and other ectoparasites. This approach parallels human probiotics that provide inner health for prevention of gastrointestinal diseases and parasites.

The aim of 'Probio-TICK – Tick control Nature's way' is to develop a safe, sustainable, cost-effective, chemical residue-free treatment for the control of cattle tick in northern Australia. Probio-TICK is designed as a cohort of microbes, applied to the hide of cattle, that will interfere with the pest's ability to mature and feed on cattle. Successful development of Probio-TICK has the potential to reduce animal handling, improve animal health and welfare, and improve environmental outcomes. Probio-TICK is a conceptually novel, first-in-class product.

1.2 Previous Research and Development

The invention of Probio-TICK arose from a joint MST, MLA and CRC-P project (B.AHE.0321) undertaken from 2017 – 2020. Probio-TICK is protected by patent. Proof-of-concept field trials conducted during the CRC-P consistently demonstrated that Probio-TICK reduces tick numbers in cattle facing natural challenge thus opening a way to a natural, chemical-free approach to tick control.

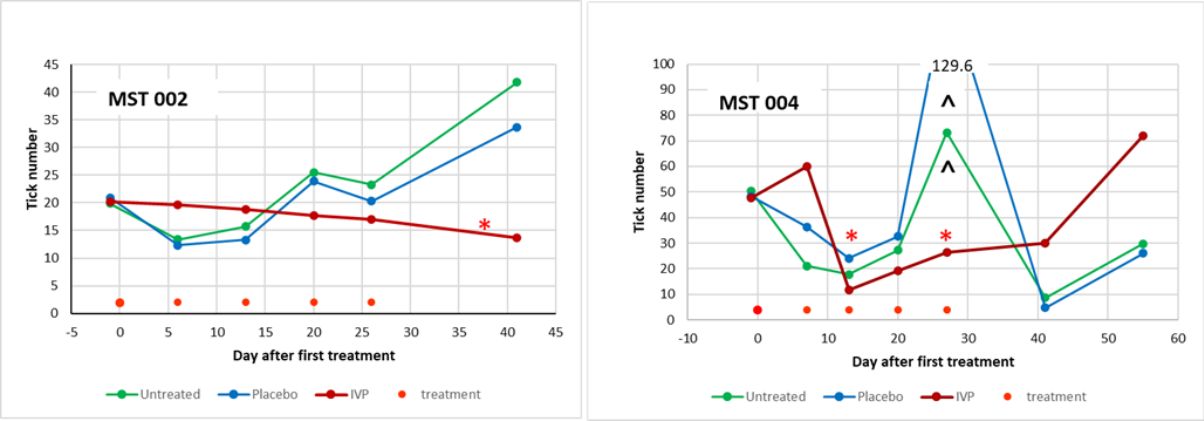
During proof-of-concept studies, MST identified a collection of microbial organisms, endemic to northern Australia, that demonstrated acaricidal and chitinase activity *in vitro*. Chitin is a critical

structural protein present in most life cycle stages of ectoparasites and the enzyme chitinase disrupts chitin structure and tick tissues.

Formulations containing between 5 and 9 microbial isolates were used in three different field trials in which cattle were exposed to natural field tick challenge. The randomised, placebo-controlled trials were undertaken in northern Queensland following WAAVP guidelines (Holdsworth PA et al 2005. Veterinary Parasitology DOI: 10.1016/j.vetpar.2005.11.011). Each of the three formulations consisted of a mixture of 5 to 9 *Streptomyces* bacterial isolates (10^9 to 10^{12} colony forming units (CFU)) in 100 mL/100g oil, aqueous vehicle or diatomaceous earth, respectively, were applied weekly on 5 occasions. Tick counts and general health assessments were undertaken on treatment days, and 2 and 4 weeks following the last treatment.

For the oil-based backliner (trial code MST 002) tick burdens declined from Day 20 compared with untreated or placebo controls, showing a statistically significant difference in favour of Probio-TICK on Day 41 (Figure 1). Cattle sprayed with the aqueous preparation (MST 004) had significantly lower tick counts on Days 13 and 27; on average across Days 13, 20 and 27 tick counts were reduced by half, with a 73% reduction on Day 27 alone. On Day 27, 4 of the 20 cattle in the control (untreated) groups were rescue treated with a chemical acaricide because of excessive tick burdens (>150 ticks on one side) (Figure 1). The trial of the powder formulation (MST 007) was commenced when natural tick burdens were low and they remained low throughout the trial (data not shown). Nevertheless, there was a modest (41%), but statistically significant, difference between the treatment and control groups was found at Day 17. These data were presented at WAAVP 2021.

Figure 1. Activity of oil-based (MST 002) and aqueous (MST 004) formulations against ticks during natural field challenge.



The proof-of-concept trials provided the first evidence that a sustainable microbial probiotic can be developed that will provide protection against cattle tick. Onset of effect occurred in about two weeks and had a persistent effect lasting for two weeks past the final treatment. There was no effect on tick egg production or viability. It is assumed the microbes affect development and/or establishment of tick larvae.

These trials demonstrated no toxicity to cattle and no environmental impacts due to Probio-TICK.

This MDC project aimed to further develop the scientific and commercial credentials of the product with scientific studies focussed on further improving efficacy through microbe refinement and scale-up of production to develop a GMP (Good Manufacturing Practice) preparation for use in stability studies and further field trials. The commercial aims included documenting the regulatory pathway to obtain marketing approval for Probio-TICK as a first-in-class and using the planned trials for

industry consultation by adoption experts. The business case was also planned to include a production methodology including cost of goods, ideal form of presentation (e.g. spray or powder) and size of market. The overall aim was to produce a body of work to the point where licencing of Probio-TICK by a commercial partner is attractive.

2. Objectives

The original objectives of this project were to:

1) Refine microbe selection to reduce the number of isolates and optimise efficacy
2) Formulate a preferred presentation for field use
3) Scale up production and manufacture a pilot batch of Probio-TICK to GMP standard that is feasible for local commercial manufacture
4) Perform product stability testing over 18 months' storage
5) Perform two field efficacy and safety trials with the selected GMP formulation, conducted according to APVMA guidelines and covering two annual tick cycles.
6) Determine the appropriate regulatory pathway for approval of Probio-TICK.
7) Undertake industry consultation to document the industry need, the preferred means of product application and tailor the integration of Probio-TICK into management systems across the tick endemic regions across Northern Australia. This will inform the adoption plan.
8) Develop a business case to attract third parties in investing in a commercial licence for Probio-TICK.

Objective #1 was met by 30 September 2021, with three microbial strains selected for Probio-TICK active pharmaceutical ingredient (API).

Objective #2 was met in April 2022, with a decision to proceed with a powder formulation for reconstitution as an aqueous spray for topical application to cattle.

Objective #3 was met in May 2022, with a pilot batch of Probio-TICK finished product (FP) manufactured by a Contract Manufacturing Organisation (CMO) and samples provided for product testing to an accredited testing laboratory.

Objective #4 has been met to date. Stability testing commenced in May 2022 and will continue after the conclusion of this project.

Objective #5 has been met to date. The first of the dose determination and efficacy trials was reported in October 2022.

Objective #6 was completed in May 2022, ahead of schedule.

Objective #s 7 and 8 have not been achieved due to the decision to terminate the MDC project at the GO/NO GO decision point (December 2022).

3. Methodology

Methodologies were appropriate and efficient, allowing MST to fulfill the project objectives.

3.1 Active Pharmaceutical Ingredient

For the purpose of developing a commercially-acceptable API (active pharmaceutical ingredient) and in line with the project objectives, MST undertook studies aimed at optimising the microbial components. This comprised: reducing the number of microbial isolates, selecting isolates most likely to have antiparasitic characteristics in the field, selecting those with low mammalian cytotoxicity *in vitro*, selecting those that grow well in culture, do not compete with each other during growth (such as on cattle skin), remaining viable on cattle skin and tolerating freeze drying. The growth process had to be scalable for pilot production and
and for a future commercial product.

In order to balance efficacy and cost considerations, MST targeted an API containing a maximum of three microbial isolates. In successful proof-of-concept trials, MST used between five and nine microbes in the API, however costs for development, regulatory approval and manufacturing of each microbe are additive. Since the contribution of each microbe to efficacy in the field is unknown, using multiple isolates poses a lower risk than using just one isolate and is the strategy commonly used for human probiotic products.

To finalise the microbial isolates that comprise the API, those isolates used in the pilot studies were ranked according to growth rate, spore stability, *in vitro* activity (activity against ticks and mites, chitinase activity, low mammalian toxicity) and our ability to recover the particular isolate from the hide of cattle during pre-MDC pilot studies. These longer living microbes are expected to have an extended antiparasitic effect.

The compatibility (lack of competition during growth) of the three selected isolates was assessed by inoculating them on one culture plate in a triangular pattern plate and examining growth zones and effects on sporulation of their neighbours.

Production of the selected strains was optimised by testing different seed media and fermentation conditions. Growth conditions were tested on GYMS and ISP2 for better sporulation. Fermentation was undertaken on cracked wheat, basmati rice and pearl barley for 14 days at 28^{o}C for comparison of spore production.

MST experimented with a number of methods to maximise the efficiency of freeze-drying, required for the final API. Experiments were undertaken to define the optimum method for mixing the strains to ensure homogeneity of the API.

The protocol for testing and release of API for manufacture into the finished product (FP) was documented.

3.2 Finished Product Formulation

The formulation of the Probio-TICK finished product (FP) was selected based on in-house rating of scientific, logistic and end-use parameters. The protocol for testing and release of FP was documented.

3.3 GMP Production

A Contract Manufacturing Organisation (CMO) was required to manufacture of Probio-TICK FP for use in field trials and stability studies. Three CMOs were assessed for their capability and capacity, including GMP license, ability to handle Streptomyces species, solid phase mixing in small batch size,

suitable storage of stability samples, Quality Control laboratory able to undertake identity and potency testing, and acceptable lead-time.

Packaging was selected on the basis of being a flexible, strong, sealable bag with sufficient volume to allow reconstitution of the FP with water prior to application on cattle. In order to maximise product stability and safety the packaging had to be suitable for food contact (Australian Standard 2070), contain no hazardous chemicals and be impermeable to air and water.

Manufacturing batch records were developed.

3.4 Stability Testing

Following APVMA guidelines for biological agents, a stability protocol was developed for testing of the API and FP. API and FP were stored at 30^{o}C and 40^{o}C in the selected packaging with test points at 0, 3, 6, 9, 12 and 18 months. Testing was undertaken at an accredited, GLP laboratory.

The methodology was appropriate for establishing stability of the materials on storage. The original stored samples are available for future testing. MST will continue stability testing in-house following completion of the MDC project.

3.5 Field Trial

The first field trial was designed as a dose-determination study with the aim of finding the lowest effective dose for use on cattle so that animal exposure is minimised and production costs of the FP are appropriate. This trial also provided safety data.
The protocol was titled 'Dose Determination of Probio-TICK Gen IV administered in an aqueous carrier topically to cattle against naturally occurring infestations of *Rhipicephalus australis* under Australian Field Conditions'. The study was undertaken by a Contract Research Organisation (CRO) and coded MST 008. The investigational product was reconstituted in an aqueous carrier prior to each use at the farm and administered topically to cattle at weekly intervals on seven occasions under Australian field conditions. The dose used in proof-of-concept trials was taken as the pre-planned target dose for Probio-TICK and 0.5x, 1.0x and 2.0x of the target dose was tested.

Six animals were included in each of five treatment groups:

- Group 1 – untreated control
- Group 2 – placebo (vehicle, diatomaceous earth (DE))
- Group 3 – 5 x 10^8 CFU per 15g application
- Group 4 – 1 x 10^9 CFU per 15g application
- Group 5 – 2 x 10^9 CFU per 15g application.

The data collected were tick counts, skin health and condition of study animals during and after the period of treatment and the acaricide resistance status of cattle tick. Protocol assessments were scheduled on Days -1, 0, 1, 7, 14, 21, 28, 35, 42, 56 and 63. IVP application was scheduled on Days 0, 7, 14, 21, 28, 35 and 42. Skin swabs were to be taken from cattle treated with the active formulations at Days -1/0, 42, 49, 56 and 63 in order to measure the persistence of applied microbes on cattle skin.

For statistical analysis of the primary trial data, tick counts were fitted to a negative binomial and analysed using a generalised linear mixed model. Pair-wise comparisons of group means were undertaken. The % reductions of treatment group means cf. the untreated control mean were tested. A statistician was contracted to analyse the results.

The methodology was appropriate and efficient, allowing MST to fulfill the project objective. In the event, a small number of protocol deviations occurred due to the impact of COVID on scheduling. The trial outcomes were still achieved.

3.6 Tick Resistance Assays

Ticks collected from animals at the study site were sent to Biosecurity Queensland Veterinary Laboratories (Coopers Plains QLD) for tick chemical resistance testing. 'and '. A panel of chemicals were used as test agents in the 'Acaricide bioassay by the larval packet test', namely cypermethrin, flumethrin, moxidectin and amitraz. For the 'Adult Immersion test for detection of resistance', fluazuron was used.

3.7 Regulatory Pathway

APVMA pre-application assistance was sought for technical advice regarding the content of planned marketing approval applications.

4. Results

4.1 Active Pharmaceutical Ingredient

Three microbial strains were selected from MST's proprietary microbial library for the final API. The strains were isolated from Queensland, Western Australia and the Northern Territory, respectively, and were active against ticks and/or buffalo fly *in vitro*, had chitinase activity, low cytotoxicity, high production, good stability and were shown to persist on the hide of treated cattle.

Optimisation experiments showed that GYMS media was preferred for MST-191872 and ISP2 media for MST-153818 and MST-152218. Jasmine rice was the optimum production media based on quantity of spores produced. Scale-up of 1.5 kg of rice yielded between 150 g - 200 g of spore powder, sufficient to provide at least 100 doses of finished product.

After experimenting with a number of freeze-drying alternatives, an effective large-scale freeze-drying method was established by snap-freezing the suspension in a dry ice/methanol bath while rotating the vessel. This created a larger surface area, thus reducing freezing time from two weeks to three days.

Approximately 800 grams of API was manufactured for the stability program and the field trial batch using the method described in 4.1 above. API contains a ratio of 25:25:50 of MST-191872, MST-153818 and MST-152218. This ratio was determined by the relative growth rate and thus availability of spores. MST-152218 was the most active grower.

Standard operating procedures (SOPs) were developed for API manufacture and testing (SOP MST 008). Product potency (CFU per gram of spore powder) was measured using spore powders resuspended in sterile water and 10-fold serial dilution to between 10^6 and 10^8. The dilutions were inoculated onto ISP2 agar plates and incubated at 28 °C for three days.

The release specification for the API was identity and potency (CFU). The potency of API tested at the accredited laboratory met specification. . Examination of Sequences of the Internal Transcribed Spacer gene of the three microbes, showed the isolates were non-identical *Streptomyces* species,

none of which are marketed in other formulations and one of which is an unreported (i.e. novel) species.

Additional work undertaken to assess the compatibility of the three microbial strains showed minimal interference in the spread of neighbouring isolates across the plate. As a result, the microbial strains are expected to be compatible in formulation and application.

4.2 Finished Product Formulation

After reviewing the proof-of-concept field trials, feedback from field trial investigators, the logistics and relative costs of manufacturing, advice from manufacturers of other registered biological agents, shelf-life, shipping, and reconstituting and applying the formulations in the field, the preferred FP was determined as a simple mixture of the API in diatomaceous earth to give a target dosage of 1 x 10^9 CFU per dose per animal based on previous studies. The formulation is the same as that used for pilot studies, with the exception that only 3 microbial strains are used. The FP was formulated at 1.3 x 10^9 microbes per dose.

After shipping to the field site, the powder concentrate was diluted with water to provide nominal 1 x 10^9 CFU per 100 mL dose of mixture containing the three microbial strains and sprayed on the hide of each animal on each occasion.

FP manufacturing and testing protocols were finalised in April 2022.

The release specification for FP was potency as measured by CFU. Specifications were set to achieve an individual target dose of 1 x 10^9 microbes. An overage of 50% and an underage of 5% was allowed, so that the specified microbe number is in the range of 0.95 and 1.5 x 10^9 CFU per dose.

In the future, the specifications for API and FP will be expanded to include appearance, moisture and other relevant parameters.

4.3 GMP Production

A GMP agreement was signed with the preferred manufacturer in December 2021. A GLP laboratory was selected as the supporting analytical laboratory, since they were already contracted to provide similar services to other companies who market biological products for veterinary use.

FP manufacture was performed at the CMO in May 2022 and testing subsequently undertaken at the GLP laboratory.

Probio-TICK FP was packaged into 500 mL, foil-lined, laminated, zip-locked pouches made of PET/PE (polyethylene terephthalate/polyethylene), thickness 140um, supplied by The Pouch Company Pty Ltd. The pouches complied with Australian Standard 2070.

4.4 Stability Testing

Stability testing of the API and FP commenced in May 2022. The six-month stability samples are currently being analysed.

4.5 Field Trial

A contract with the CRO was executed in March 2022. QDAF Ethics Committee approval was obtained on 14 March 2022 (approval # SA 2022/03/822). The study was conducted as a small-scale trial under the APVMA general permit PER 7250. The report of the field trial was completed on 14 October 2022.

The herd of cattle used in the study comprised animals with a predominance of *Bos taurus* genetics over *Bos indicus*. The in-animal phase of the trial was undertaken between 18 May and 28 Jul 2022 on the Atherton Tablelands, QLD. There were several deviations to the trial schedule caused by COVID isolations affecting study personnel. Treatment application and assessments were rescheduled to Days -1, 0, 14, 19, 29, 35, 41, 49, 56, 61 and 70 (cf. planned schedule of Days -1, 0, 1, 7, 14, 21, 28, 35, 42, 56 and 63).

Tick numbers confirmed that there was adequate challenge with ticks during the trial period. Tick burdens fell in all groups as the trial progressed. For example, in the control group the means were 39.7 on Day 0 and 7.5 on Day 70. Probio-TICK was successfully applied to the cattle. Rescue treatment with acaricide for a high tick burden was required and followed the gap in treatment described above.

Analysis of group mean tick counts (fitted to the negative binomial) showed that there were statistically significant reductions in tick counts between the treatment Groups and the control Group, but no dose-response was seen (Figure 2). For each IVP-treated Group lower counts were found on 3 out of 4 sampling days from Day 49 to Day 70. For the 0.5x dose significant reductions occurred on Days 49, 56 and 61 (% reductions of 54.4, 89.5 and 62.2, respectively). For the 1x dose significant reductions occurred on Days 49, 56 and 70 (% reductions of 73.5, 77.7, 85.6, respectively). For the 2x dose significant reductions occurred on Days 49, 56 and 61 (% reductions of 77.9, 81.9, 61.8, respectively). By comparison the Placebo (DE) group (Group 2) showed a significant reduction compared with the control on only one day (Day 56; 67.1% reduction).

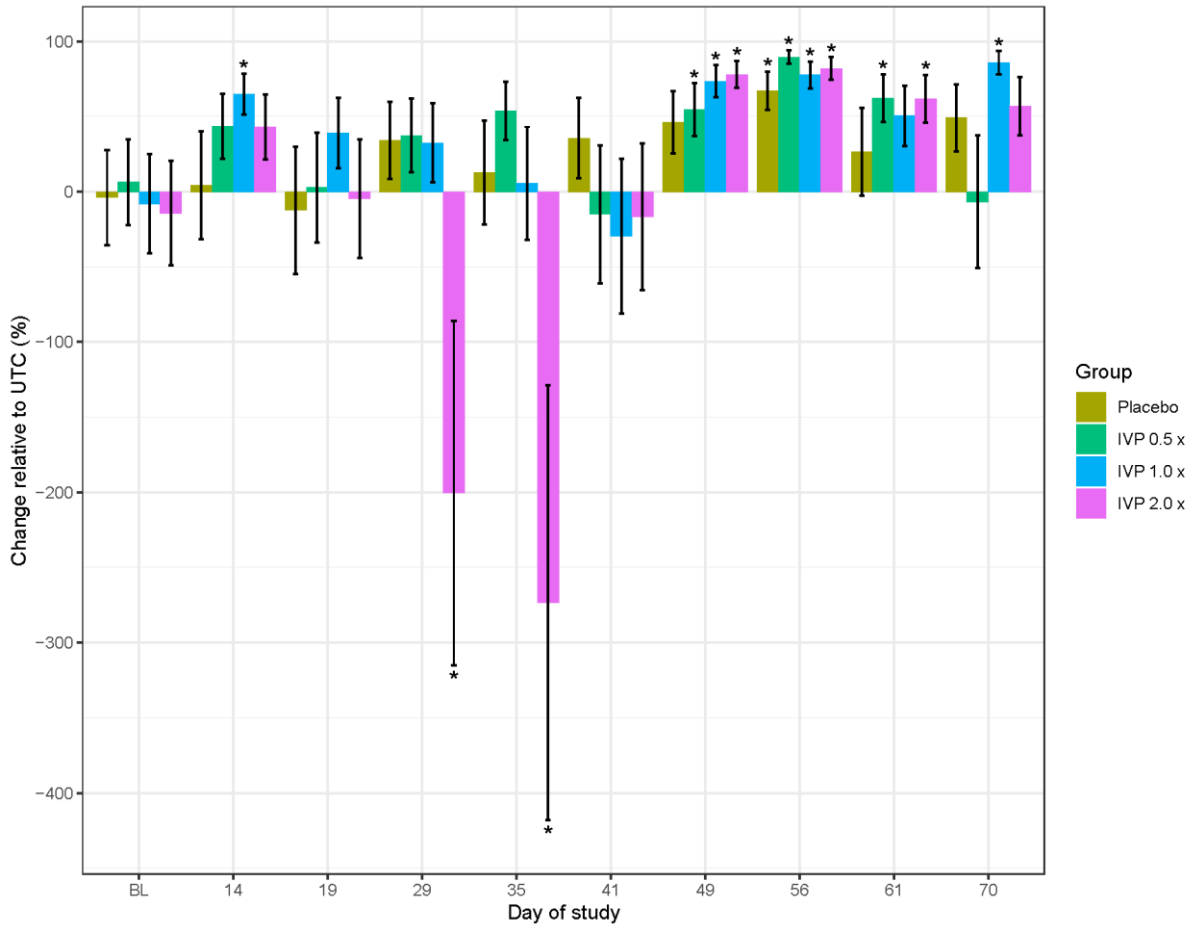
The final treatment was applied on Day 49. The effects of the IVP persisted in the treated groups (indicated by significantly lower tick counts) for 12 days (Day 61) to 21 days (Day 70) post treatment.

No adverse events, including dosing site effects, were reported during the study and the IVP did not adversely affect the general health of any of the animals. Analysis of ticks from the study site indicated that there was no resistance to amitraz or macrocyclic lactones, but high-level resistance to fluazuron. Analysis of the skin microbiome to measure the persistence of applied microbes is pending.

The data support the contention that Probio-TICK is safe and may have a role to aid the control of cattle tick. Although a dose-response was not demonstrated, the selected dose of 1×10^9 is reasonable.

The COVID-19 pandemic had an impact on this study by delaying one early treatment. It is likely that this led to a delay in the reduction of tick numbers following treatments. In previous studies tick burdens commenced their decline 2 to 3 weeks after weekly treatments commenced. In the current trial the delay was up to 49 days. These data suggest that weekly treatment is the appropriate interval for field use.

Figure 2. Model-based % change in mean tick counts of the four treatment groups compared with the control (UTC), over the 10 time points. Error bars are standard errors. Study day 'BL' indicates base line Days -1 and 0 combined. Within a study day, % change values with an asterisk (above or below the error bars) indicate a significant difference from the control (P < 0.05).



4.6 Regulatory Pathway

MST proposed that to support the claim of 'aids in the control of cattle tick', a target of 50% reduction in tick burden was appropriate to demonstrate efficacy.

MST received AVPMA's advice in May 2022. The majority of APVMA's advice was reasonable and, where applicable, allowed scientific argument in the place of formal studies (e.g. for the majority of toxicological requirements, scientific argument could be made for omitting these studies). However, the APVMA set a high bar for demonstrating efficacy, including applying the WAAVP Guidelines (Holdsworth PA et al 2005. Veterinary Parasitology DOI: 10.1016/j.vetpar.2005.11.011) which are designed for chemical agents rather than biological control agents such as Probio-TICK.

The report indicated that the product needed to demonstrate satisfactory stable levels of tick management over long term field use including greater than 95% efficacy.

This advice effectively precludes Probio-TICK from being registered as a stand-alone product in Australia and a hold on development of Probio-TICK is in place.

Probio-TICK is protected by Australian and International patents. New national phase applications have been submitted in Brazil and South Africa where it is hoped that the regulatory requirements for Probio-TICK are more pragmatic.

5. Conclusion

5.1 Key findings

MST, in its collaboration with MLA and through the current project, has further demonstrated that a cohort of microbes, selected for their *in vitro* activity against ectoparasites and applied topically, reduces the tick burden in cattle exposed to natural field challenge. Reducing the number of microbes in the formulation to three still produces consistent field results.

We believe that this product which has consistently reduced tick burdens in *Bos taurus* cattle has a future application to aid in control of ticks on all types of cattle. It would be especially useful in enterprises that value chemical-free control.

MST has further demonstrated that GMP manufacture of the API and FP is feasible and will be cost-effective. The long-term stability of the API and FP has yet to be confirmed.

The current regulatory stance precludes Probio-TICK from being developed as a stand-alone product in Australia at this time.

5.2 Benefits to industry

The project has reinforced the potential benefits of the Probio-TICK microbes to aid in control of ticks in Northern Australia. The opportunity for organic control is attractive in markets where chemical use is preferred or mandated.

Unfortunately, the regulatory environment at this time is not flexible enough to consider biological products outside the guidelines designed for use of chemicals necessitating a different approach to the development of Probio-TICK.

6. Future research and recommendations

MST intends to further investigate the viability of marketing approval applications of Probio-TICK in jurisdictions overseas, especially for those in which it holds patents and for application as an ectoparasiticide in other industries. Papers describing this research will be submitted for publication in 2023

7. References

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