GALVmed

Protecting Livestock – Improving Human Lives

East Coast Fever Infection & Treatment Method

East Coast Fever – The Disease

East Coast Fever (ECF) is a disease of cattle caused by a blood-borne protozoal parasite, *Theileria parva*, predominantly carried by the brown ear tick (*Rhipicephalus appendiculatus*). It causes significant economic losses across East, Southern and Central Africa through death and production losses. In exotic dairy cattle, mortality rates are typically very high, but high mortality may also be experienced in pastoralist calves and cattle not previously exposed to the disease. The disease is reported in 11 countries in Africa and annual losses associated with ECF have been estimated at more than $300m per annum (ILRI Research Brief 09/14).

East Coast Fever – Existing Methods of Control

East Coast Fever is currently controlled by three means:

1 Prevention of Disease using Acaricides

Acaricides, chemicals applied to animals by dipping, spray or by pour-on, are well established in their use to reduce or eliminate tick colonisation of cattle. Various chemical classes are used. The advantage of acaricides is that they control all tick species, thereby controlling all tick-borne diseases, as well as reducing hide damage. The concerns about use of acaricides include significant resistance issues leading to poor efficacy or increased frequency of use, high cost and environmental impact. Of course, acaricides do not prevent disease transmission to cattle if an infected tick survives treatment due to resistance or under-dosing.

Even if ECF is controlled by other means, the need for acaricides may remain, to ensure control of other tick-borne diseases such as Heartwater and Anaplasmosis. However, in most situations, the frequency of use can be significantly reduced.

2 Treatment of Disease using curative drugs: Parvoquone and Buparvoquone

Two related molecules are licensed for treatment of ECF. Treatment can be effective if administered early in the disease, but the cost of treatment is high.

Accurate differential diagnosis in the field is difficult and may lead to inappropriate or delayed treatment. In animals affected by environmental stress factors, such as poor nutrition, these drugs can be sufficiently toxic to lead to death of the treated animal.

3 Prevention of Disease by vaccination using the Infection Treatment Method (ECF-ITM)

This procedure involves concurrent injection of a measured dose of live parasites and an antibiotic, 30% oxytetracycline, to control the resulting disease. The product exposes the animal to a controlled dose of the disease which, due to control by the antibiotic, occurs without any clinical signs while allowing the animal to build long-term immunity to ECF.

All means of controlling the disease have their place, but clearly disease prevention is preferable to treatment.

ECF Infection & Treatment (ECF-ITM) Approach

The ECF-ITM approach, which typically provides life-long immunity, comprises a single dose vaccine ideally given to calves, by injection close to the parotid lymph node behind the ear, which is the natural attachment site for the ticks. Concurrent with vaccination, the animal is injected with an antibiotic, 30% oxytetracycline, which limits the effect of the parasite, allowing development of an immune response without significant clinical effects.

Vaccinated calves are ear tagged to identify that they have been vaccinated. They may also be given a dewormer concurrent with vaccination.

The ECF-ITM method has been safely and effectively administered over a long period, having provided effective protection in more than 1 million animals. There is, however, significant opportunity to increase uptake. The full treatment is expensive (currently between US $6 – 10 per animal) but given the high levels of disease incidence and post-infection mortality in endemic areas, the price is not usually considered a constraint. Indeed, considering the costs of alternative methods of control and the overall value of the live animal, ECF-ITM is considered fair value.

History of ECF-ITM

The ECF-ITM method was developed in the 1970s by the East African Veterinary Research Organisation, in conjunction with numerous partners. The vaccine currently produced, often known as the Muguga cocktail, is a combination of three parasite strains found in East Africa.

The first commercial vaccine batch was manufactured in the 1990s at the International Laboratory for Research into Animal Diseases (ILRAD; now the International Livestock Research Institute, ILRI), under funding from the UN Food & Agriculture Organisation. A subsequent batch was produced by ILRI in 2008 which has been used in East Africa until recently, when stocks ran out due to significant demand from small-scale farmers and pastoralists.

Since 2011, ILRI has assisted GALVmed in a manufacturing technology transfer, including transfer of ticks, seed stock and know-how, to the Centre for Ticks & Tick-Borne Diseases (CTTBD) in Lilongwe, Malawi. This organisation was selected as the manufacturing site following open tender, by a team of senior representatives from the national governments impacted by ECF under the guidance of the African Union. The centre, which has a pan-African mandate for training and diagnosis of ticks and tick-borne diseases, also had a history of producing single strain theilerial vaccines for supply to Zambia and Zimbabwe.

Production of ECF-ITM vaccine has now started at CTTBD and the product is available for purchase.

GALVmed's Involvement: Partnership with the Centre for Ticks & Tick-Borne Diseases

Reliability of supply and quality of product has been a major constraint in the uptake of the ECF-ITM approach. GALVmed's partnership with CTTBD seeks to address these issues. GALVmed's approach has been holistic, focussing on a number of perspectives:

- Ensuring vaccine availability from CTTBD with support in technology transfer and quality control from ILRI in Nairobi, Kenya
- Enhancement of a dedicated vaccine production facility at the CTTBD
- Building delivery capabilities (vaccinator training) and market awareness (field days etc.)
- Official product registration in three countries to date
- Process improvements to ECF-ITM vaccine
- Assisting in supporting CTTBD's supply chain and marketing capabilities
- Advocacy for use of ECF-ITM at government level
- Collaboration with the African Union Commission in building organisational capacity

It is worth stressing that, while GALVmed supports vaccine production and stimulates market awareness for the product, vaccine sales occur solely through commercial links between CTTBD and CTTBD-appointed independent commercial distributors and, in some cases, government veterinary services.

Ensuring vaccine availability

Although the vaccine has been available for an extended period, the number of commercial batches produced has been few. Infrequent production and availability has limited product use and lowered customer confidence. Limited efforts have been made to enhance uptake due to this infrequent availability. GALVmed is seeking to address both aspects by ensuring product supply and creating increased market demand. GALVmed does not sell or administer vaccine itself.

Enhancement of a Dedicated Vaccine Production Facility

With major support from its funders, the Bill & Melinda Gates Foundation and the UK Government, significant investments have been made by GALVmed to upgrade the existing centre to create a facility suited to reliable production of theilerial vaccines for affected countries. This involved investment in infrastructure, provision of equipment and training programmes. In addition to annual supply of single strain vaccine to Zambia, the first batch of ECF – ITM vaccine was released for commercial uptake, in late 2014.

Despite its close supportive affiliation with GALVmed, CTTBD is an independent legal entity under the auspices of the African Union Commission, Department of Rural Economy and Agriculture.

Building Delivery Capabilities

In collaboration with CTTBD and other partners, in particular the independent commercial distributors of the vaccine at country level, GALVmed has worked to build increased awareness of ECF as a disease and the benefits of ECF-ITM in its control.

The challenges of delivering a vaccine that requires storage in liquid nitrogen to relatively remote areas is self-evident, but there are improving mechanisms to ensure accessibility in markets where the vaccine is currently available. There remains a significant amount of work to be undertaken in confirming the suitability of the ECF-ITM vaccine strains for markets outside those where the product is currently available, including South Sudan, Rwanda and Mozambique.

Administration of the vaccine requires specifically trained skilled personnel. Only accredited and registered vaccinators are allowed to administer vaccine. GALVmed assists with implementation of vaccinator training programmes through the national veterinary services and through independent commercial distributors. There remains a significant opportunity for improved and extended collaboration in this area to ensure there are sufficient vaccinators to allow product use to increase and to ensure trained vaccinators retain the required standard. Since ECF vaccine is a product farmers are able and willing to pay for, the goal is to ensure a network of reliable vaccinators across the region with sufficient economic interest in the service they offer for it to be an interesting private sector venture.

Product Registration

Despite its extensive use over many years, there had not been any concerted effort to build a complete registration dossier for the ECF-ITM product. GALVmed has assisted in compiling a comprehensive registration dossier, which was submitted through the relevant national authorities leading to full product registration in three countries and authorised use in another. With the change in site production to CTTBD, the dossier update and resubmission is required, which is ongoing.

Process Improvements

While the established vaccine production processes lead to a safe and effective vaccine, these manufacturing processes have never been optimised. The vaccine currently takes 18 months to produce, which leads to significant supply chain issues and biosecurity concerns.

A concerted effort is ongoing, in partnership with CTTBD and an independent expert advisory committee, to address areas of potential improvement of the vaccine. This includes methods for *in vitro* pre-release quality control, alternatives to the current diluent and, ultimately, finding an approach to conserve sporozoite viability without the need for liquid nitrogen storage. Improved production processes are also expected to lead to production cost reduction. The goal is to reduce manufacturing costs by at least 50%, through a combination of increased production efficiency and improved manufacturing processes.

Supply Chain & Marketing

When vaccine is available, there is a need to ensure a robust and reliable supply chain to the local distributors and to assist the distributors in creating product demand. This has never been part of CTTBD's previous function. GALVmed is assisting the centre to build these components and is currently supporting a Strategic Business Manager at CTTBD to prepare and oversee implementation of a business plan for ensured sustainability of the Centre.

The Future

Ultimately, and at the earliest opportunity, GALVmed's objective is to withdraw from active involvement in ECF-ITM vaccine, leaving in place a reliable, well-established production facility at CTTBD, with effective distribution mechanisms leading to sustainable supply and significantly increased vaccine uptake across existing and new markets based on commercial models.

Ultimately this will support a GALVmed goal, which is shared by all our partners and stakeholders: A robust contribution towards nutritional security and improved livelihood for farmers in Africa.

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