Pro-poor vaccine-based control of East Coast fever

Validated RNRRS Output.

In Central and East Africa, work is ongoing to give producers access to effective vaccines that will protect their cattle against the devastating disease East Coast Fever. This could greatly improve the lives of poor livestock keepers, as East Coast fever is responsible for about half of all calf deaths in pastoral and agro-pastoral production systems in these areas. One thrust of these efforts is the promotion of the infection and treatment method (ITM), which has already been shown to be effective but which has not been widely taken up for a variety of reasons. Other efforts are concentrating on the development of next-generation vaccines that are safer, costs less, and are easier to transport.

Project Ref: AHP14:
Lead Organisation: International Livestock Research Institute (ILRI), Kenya
Source: Animal Health Programme

Document Contents:

Description, Validation, Current Situation, Current Promotion, Impacts on Poverty, Environmental Impact,

Description

AHP14
A. **Description of the research output(s)**

1. **Working title of output or cluster of outputs.**
   *In addition, you are free to suggest a shorter more imaginative working title/acronym of 20 words or less.*

   Short title: Pro-poor vaccine-based control of East Coast fever

2. **Name of relevant RNRRS Programme(s) commissioning supporting research and also indicate other funding sources, if applicable.**

   - RNRRS Programme: Animal Health Research Programme
   - Decision support for risk management strategies of tick-borne diseases within sustainable pastoral systems-R8208
   - Integrated Control of East Coast fever constraining livelihoods of smallholder farmers in sub-Saharan Africa - R8042
   - Support For Deployment Of Live Vaccine against ECF - R6725H

   **IFAD funded**
   - Enhancing the impact of immunisation against East Coast Fever with an improved sub-unit vaccine on the smallholder dairy sector in eastern Africa-TAG376
   - Infection and Treatment Method at the Crossroads: Project Addressing Key Constraints to the Sustainable Delivery and Adoption of Immunization Against East Coast Fever for Poor Livestock Keepers in Eastern Africa-TAG376

   **World Bank, Agricultural Research Fund**
   - Pilot delivery of ITM using the Muguga Cocktail in the Narok district of Kenya

   **FAO funded**
   - Contractual services agreement with ILRI for “Preparation of a composite stabilate for FAO” – funding support also provided by ILRI.

3. **Provide relevant R numbers (and/or programme development/dissemination reference numbers covering supporting research) along with the institutional partners (with individual contact persons (if appropriate)) involved in the project activities. As with the question above, this is primarily to allow for the legacy of the RNRRS to be acknowledged during the RIUP activities.**

   - R8208: Decision support for risk management strategies of tick-borne diseases within sustainable pastoral systems
     
     **Partners:**
     - Graham Medley, University of Warwick (Principal Investigator);
     - Lieve Lynen, ITTBDP, Arusha, Tanzania
     - Guiseppe Di Giuglio, ITTBDP, Arusha, Tanzania
     - Paul Gwakisa, Sokoine University of Agriculture, Morogoro, Tanzania;
The cluster of outputs were aimed at better control of one of the most devastating cattle diseases in East and Central Africa; **East Coast fever (ECF)**. Some outputs relate to better application of an existing vaccine while others look at improving the impact of immunisation against East Coast Fever with an improved sub-unit vaccine on the smallholder dairy sector in eastern Africa.
others relate to the development of an improved vaccine. ECF is a disease of cattle widespread in 11 countries in East, Central and Southern Africa. It is transmitted to cattle through the bites of the tick *Rhipicephalus appendiculatus*. Of the estimated 40 million cattle in this region, about 26 million are at risk of ECF. ECF is responsible for about half of all calf deaths in the pastoral and agropastoral production systems and is largely responsible for the lack of upgrading of indigenous breeds in areas where it occurs. Current ECF control strategies include regular use of acaricides or treatment of sick animals both of which have been unsuccessful. The **infection and treatment method** (ITM) of immunisation was developed in the mid 70s. It involves inoculation of cattle with live parasites together with a long-acting antibiotic that leads to mild reaction and full immunity against subsequent infection. Although ITM is highly effective it has some limitations including the need for a cold chain, high cost and concerns of safety. There is therefore, a need to develop an improved vaccine.

**Outputs related to the impact of ITM:** Information has been gathered on the impact of ITM in different cattle production systems. Concerns related to the safety of the vaccine and long-term biological impacts have been addressed thus allowing policy changes that have promoted the use of ITM as central strategy for ECF. Availability of molecular tools for ECF parasite characterisation have assured policy makers and service providers that long-term impacts of the use of a live vaccine across the regional can be monitored.

**Outputs related to commercialisation initiatives.** Research based evidence from pilot studies have demonstrated the commercial viability of ITM. This has influenced policy-makers to allow the use of the vaccine in Kenya, Uganda and Tanzania. It has also created interest by the pharmaceutical companies in investing in the production and distribution of the vaccines. The Agrochemical Association of Kenya (AAK) and GALV-Med have shown interest in creating **public-private partnerships** with research institutes to provide access by the livestock farmers to ITM in the regional.

**Outputs related to the next generation vaccines:** The need to **develop recombinant vaccines** for ECF has arisen from the limitation of the current live vaccine with regard to safety, deliverability (cold chain) and costs. The DFID supported research on recombinant ECF vaccines has led to the following key outputs:

- Assembly of an international consortium embracing diverse expertise and experience, with public-private partnerships.
- Drawing on the latest advances in science and technology especially in genomics and bioinformatics to address a local problem.
- Identification of potential **antigen candidates** for vaccines.
- Publication of results in top peer-reviewed journals.

5. **What is the type of output(s) being described here?**

Please tick one or more of the following options.

<table>
<thead>
<tr>
<th>Product</th>
<th>Technology</th>
<th>Service</th>
<th>Process or Methodology</th>
<th>Policy</th>
<th>Other</th>
<th>Please specify</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>X</td>
<td>X?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6. **What is the main commodity (ies) upon which the output(s) focussed? Could this output be applied to other**
RESEARCH INTO USE PROGRAMME: RNRRS OUTPUT PROFORMA

commodities, if so, please comment

The outputs focus on livestock and livestock products

ECF vaccine research represents an excellent example of a rational approach to development of robust vaccines against complex pathogens. Central to this approach is the availability of a strong platform of immunological information on host protective immune mechanisms and a good knowledge of the biology of the pathogen. The technical success of developing a subunit vaccine against ECF is hinged on excellent progress in identification of antigens which are targets of the well-characterised host immunity based on CD8 T cell responses. Equally important, is the identification of an effective vaccine formulation which will induce such immunity against lethal challenge. The availability of a *T. parva* genome sequence, a good quality schizont cDNA library and availability of a high throughput antigen screening system have underpinned the success in identifying bonafide vaccine candidates.

By virtue of their intracellular location in nucleated cells, pathogens that cause *malaria*, *TB*, *tropical theileriosis* and *heartwater* (all major killers) are targets of the CD8 T cell immunity similar to that in ECF. It would therefore be expected that similar strategies could be employed to identify target vaccine candidates. It is of great benefit that the genomes of all these pathogens have been sequenced and are either fully annotated and published. As the project is using the same vaccine formulations (DNA/MVA prime/boost) which are being evaluated in human clinical trials for TB and malaria, opportunities for information exchange are being exploited towards the realisation of global public goods. Immortalisation of *Theileria*-infected host cells is reminiscent of a cancerous state. Human cancer studies have shown that CD8 T cells are also important in resolution of tumors suggesting that similar vaccine approaches can be employed. In addition, the availability of a fully annotated *T. parva* genome sequence will inform studies on the transformation of the infected host cell which might provide clues to mechanisms in cancer. The publication of these data would be yet another example of global public goods.

**7. What production system(s) does/could the output(s) focus upon?**

Please tick one or more of the following options. Leave blank if not applicable

<table>
<thead>
<tr>
<th>Semi-Arid</th>
<th>High potential</th>
<th>Hillsides</th>
<th>Forest-Agriculture</th>
<th>Peri-urban</th>
<th>Land water</th>
<th>Tropical moist forest</th>
<th>Cross-cutting</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**8. What farming system(s) does the output(s) focus upon?**

Please tick one or more of the following options (see Annex B for definitions).
Leave blank if not applicable

<table>
<thead>
<tr>
<th>Smallholder rainfed humid</th>
<th>Irrigated</th>
<th>Wetland rice based</th>
<th>Smallholder rainfed highland</th>
<th>Smallholder rainfed dry/cold</th>
<th>Dualistic</th>
<th>Coastal artisanal fishing</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**9. How could value be added to the output or additional constraints faced by poor people addressed by clustering this output with research outputs from other sources (RNRRS and non RNRRS)? (max. 300 words).**
Although most fail points for commercial and sustainable delivery of ITM have been addressed through the outputs described above there remains some constraints to this process. Linkages of these outputs with trade issues to allow for non-restrictive trade among the countries in the region would add value to this output.

Although commercialisation has been identified as best option of the sustainable delivery of this technology this does not benefit all segments of the poor farmers equally. Linking this output with other support to disadvantaged farmer groups such as micro credit schemes would greatly add value to the output.

Since ITM has such a dramatic reduction in calf mortality, value would be added by addressing marketing constraints for livestock and livestock products so that farmers fully benefit from reduced losses through higher offtakes. Linking this output with a marketing project or livestock producer organisation would add value to the output.

Please specify what other outputs your output(s) could be clustered. At this point you should make reference to the circulated list of RNRRS outputs for which proformas are currently being prepared.

The output would complement and could be clustered with the AHP outputs Decision support for diagnosis: Simple decision support tools for diagnosis of endemic diseases in Africa and Treatment of cattle to eliminate the animal reservoir of T.b. rhodesiense.

---

Validation

B. Validation of the research output(s)

10. How were the output(s) validated and who validated them?

Please provide brief description of method(s) used and consider application, replication, adaptation and/or adoption in the context of any partner organisation and user groups involved. In addressing the “who” component detail which group(s) did the validation e.g. end users, intermediary organisation, government department, aid organisation, private company etc... This section should also be used to detail, if applicable, to which social group, gender, income category the validation was applied and any increases in productivity observed during validation (max. 500 words).

Extensive validation of the ITM technology to determine safety, efficacy and impact and improve deliverability has been carried out at three levels; laboratory experimentation, controlled field immunisation, pilot projects with partial cost recovery and commercial delivery. Laboratory trials on efficacy and safety and identification of immunising parasites have been conducted by the former East Africa Veterinary Research Organisation (EAVRO), the Kenya Agricultural Research Institute (KARI) and the International Livestock Research institute.

Safety and efficacy has been determined through experimental challenges of immunised cattle, with a range of parasites to assess the spectrum of protection with non-immunised cattle as controls.
Controlled field immunisations, to assess efficacy and safety where the level of challenge is based on comparison of disease in immunised and non-immunised cattle have been conducted in Kenya, Malawi, Rwanda, Uganda, Tanzania, Zambia, Zanzibar, Zimbabwe and Rwanda. Validation has been carried out on both single (Kenya, Rwanda, Zambia, Zimbabwe) and a mixture of parasite stocks (Kenya, Malawi, Uganda, Tanzania, Zambia). Most of the trials have been conducted by national agricultural research systems with support from bilateral and multilateral donors. For instance in Kenya, KARI with support from ODA and later DFID carried most of the field trials. In Uganda the Livestock Research Institute (LIRI) with support from DANIDA conducted the trials. In Zanzibar, ILRI with funds from ODA conducted some of the field trials. In Tanzania the Integrated Ticks and Tickborne disease project with support from Dutch and Austrian government supported most of the field trials.

Pilot field immunisation have been carried out in most of these countries to assess efficacy, safety, spectrum of protection and impact of ITM. Most of these have been supported by donor project. In Southern Africa (Malawi, Zambia, Zimbabwe, Tanzania) an FAO regional project on ECF immunisation conducted most of these projects. In East Africa bilateral donor supported the work (e.g. DFID in Kenya, DA in Uganda).

Commercial validation of ITM has been carried out in Kenya and Tanzania. In Kenya Coopers Kenya limited, a private pharmaceutical company was given the exclusive rights to deliver the single stock based ITM vaccine but due to geographical and production system restriction the company was unable to sustain the delivery. More recently a non governmental organisation, Veterinares sans Frontiers Germany (VSF-G) in collaboration with KARI and ILRI has established a successful commercial delivery in the Maasai pastoral areas.

In Tanzania commercial delivery by Vetagro, Tanzania, in pastoral areas has been going for about three years with more than 100,000 cattle immunised this way.

Nearly all production systems have been involved in these trials. In Kenya and Zimbabwe the pilot field trials and commercial delivery were initially in smallholder dairy farms and large scale commercial farms. Recently commercial delivery has gone into pastoral production systems. In the rest of the region most of the trials have been in pastoral and agropastoral production systems with indigenous breeds.

11. **Where and when have the output(s) been validated?**

Please indicate the places(s) and country(ies), any particular social group targeted and also indicate in which production system and farming system, using the options provided in questions 7 and 8 respectively, above *(max 300 words).*

In Kenya validation with the single parasite stock was carried in between 1992 to 2000 at 22 sites in all parts of the country including Coast, Central, Eastern, Rift Valley, Nyanza and Western provinces. Most of the trials were in smallholder dairy rain fed highland systemsand in periurban dairy farms but a few were also conducted in large scale commercial dairy farms. More recent trials have since gone to pastoral extensive production systems which are semi arid livestock systems.

In Uganda trials were conducted between 1990 to 2002 in 29 districts covering all parts of the country. The
Validation of ITM in Tanzania was between 1989-2002 in different regions, including Iringa, Mbeya, Dar es Salaam, Morogoro, Kagera, Mwanza, Arusha, Kilimanjaro, Tanga Shinyanga, Mtwara, Lindi and Kigoma districts. Initially trials were conducted in smallholder dairy (90%) and commercial dairy (10%) but later shifted to indigenous pastoral systems 90%.

Current Situation

C. Current situation

12. How and by whom are the outputs currently being used? Please give a brief description (max. 250 words).

ITM is being delivered commercially by private veterinarians in Narok, Kajiado and Mara districts of Kenya. The private vets were initially supported to set up ITM delivery centres by VSF-Germany an international NGO. Pilot delivery by private veterinarians is also under way in medium to large scale dairy areas in Uasin Gishu districts and Laikipia districts in collaboration with the KARI and ILRI.

Vetagro-Tanzania took over delivery of ITM in Coastal areas of Northern Tanzania from ITTBD project. Currently there is also a FAO funded delivery by public sector through the Ministry of Water and Livestock Development other parts of the country.

In Uganda and Zambia ITM is currently delivered by the veterinary department. The government is responsible to sources and delivering although private vets can deliver but with approval by the government.

13. Where are the outputs currently being used? As with Question 11 please indicate place(s) and countries where the outputs are being used (max. 250 words).

ITM is currently being used in the following countries:
Kenya-Narok and Kajiado (pastoral) Uasin Gishu (dairy) and Laikipia (large scale commercial) districts
Tanzania-Arusha region-pastoral, Tanga (smallholder dairy), Southern highlands (agropastoral)
Uganda-Several districts targeting mostly smallholder dairy.
Zambia- Eastern and Southern provinces of Zambia. Mostly in agropastoral production systems.

14. What is the scale of current use? Indicating how quickly use was established and whether usage is still spreading (max 250 words).

The scale of current use can only be described as modest. Zambia has the largest number of users followed by Tanzania, and Kenya. Zambia currently uses about 50,000 doses per year making a total of about 300,000 cattle immunised since the start of the programme. Tanzania is currently using 30,000 doses and has far immunised about 200,00 cattle. Kenya is currently using about 5,000 doses per year and in the last two years since the start of commercial delivery a total 10,00 cattle have been immunised. The numbers of cattle currently immunised in
Malawi and Uganda is estimated to be low limited due to various factors including lack of promotion and commercialisation of distribution/delivery. Although there is considerable demand and use is spreading, it is hampered by a number of factors such as government restrictions, vaccine supply and service delivery. A lack of full involvement of the private sector is also a factor. It is estimated that at moderate adoption rates 10-30% a total of 1.5 million doses of an ECF vaccine could be used in the region.

15. In your experience what programmes, platforms, policy, institutional structures exist that have assisted with the promotion and/or adoption of the output(s) proposed here and in terms of capacity strengthening what do you see as the key facts of success? **(max 350 words)**

The various donor funded programmes in the region have helped in the refining of the technology to the point where it is now acceptable to all stakeholders as a safe product. ILRI technical expertise in ECF and vaccine stabilates production has played a critical in creating the necessary confidence by allaying fears due to an inadequate understanding of the epidemiology of the disease. The support by DFID to develop molecular tools for parasite characterisation and the use of these tools in the FAO supported production of the last vaccine batch which is in current use was pivotal. The presence in the region of strong NARS (KARI in Kenya, LIRI in Uganda and ITTBD in Tanzania) with well trained technical staff was also crucial in the promotion of the technology.

Use of the technology has also been assisted by the failure of previous control methods principally tick control. Due to reduced government funding in animal health subsidies in tick control have been withdrawn resulting in an inefficient tick control programmes. The development of resistance by ticks to various acaricides has worsened the problem.

---

**Current Promotion**

**D. Current promotion/uptake pathways**

16. **Where is promotion currently taking place?** Please indicate for each country specified detail what promotion is taking place, by whom and indicate the scale of current promotion **(max 200 words)**.

In Kenya promotion of ITM is taking place in the Maasai pastoral system (Narok, Kajiado and Mara districts) in Kenya. Promotion is also taking place in the dairy areas and to lesser extent in the large scale commercial beef production areas.

In Tanzania the technology is being promoted in most parts of the country through an FAO project. Vetagro Tanzania is also promoting the technology in the Arusha region of the northern parts of the country. The current promotion has supported immunisation of more than 80,000 cattle in 2006 and this number could rise to above 100,000 during this year.

17. **What are the current barriers preventing or slowing the adoption of the output(s)?** Cover here institutional issues, those relating to policy, marketing, infrastructure, social exclusion etc. **(max 200 words)**.
There are several barriers which are preventing and slowing the pace of adoption of ITM in the region:

- There is currently no entity to sustainably produce a safe reliable vaccine. ILRI produced the last batch with funds provided by FAO. It believed only the private sector can play this role in sustainable way.
- Private sector has been reluctant to invest in production until clear policies are in place. The ambivalence of some governments about the role of the private sector has slowed the adoption of the technology.
- Lack of a harmonised regional commercialisation to take advantage of the larger market has also inhibited adoption of the technology.
- Continued concerns by some stakeholders on about safety, issues related to carrier states in cattle, parasite recombination have slowed adoption.
- Technical issue such as the number of doses in bottle has been a constraint to adoption because of low number of cattle per household and the requirement to use the vaccine within a given period after reconstitution.
- The fact that the use of the ITM leads to reduction in the use of some conflicts with existing products such as acaricides and curative drugs have made some service providers reluctant to promote the technology.

18. What changes are needed to remove/reduce these barriers to adoption? This section could be used to identify perceived capacity related issues (max 200 words).

- A public-private partnership may be required, at least initially, to establish an effective production centre. The start-up costs to establish appropriate facilities, technologies and expertise are high and the private sector may be unwilling to invest in this process.
- Since the markets are fragmented by national borders and production system, a harmonised regional approach to ITM would help the technology greatly.
- A clear policy on the role of the private sector in the distribution of ITM would allow the sector to be fully involved in the technology.
- Studies to identify the impact of technology in terms of social effects would allay fears from service providers on the likely loss of business and help then promote the technology.

19. What lessons have you learnt about the best ways to get the outputs used by the largest number of poor people? (max 300 words).

- Appropriate government policies have been critical without which little progress can be made.
- Well documents science based evidence would influence decision making by policy makers.
- All the concerns of all the stakeholders must be addressed. Identifying the stakeholders and involving them at the appropriate stage is very critical.
- Institutional interests must be addressed even though quite often they might be working against national interest can be quite a problem. A suitable mechanism to either accommodate them or deal with their consequences must be sought.
E. Impacts on poverty to date

20. Where have impact studies on poverty in relation to this output or cluster of outputs taken place? This should include any formal poverty impact studies (and it is appreciated that these will not be commonplace) and any less formal studies including any poverty mapping-type or monitoring work which allow for some analysis on impact on poverty to be made. Details of any cost-benefit analyses may also be detailed at this point. Please list studies here.

- KM Homewood, Anthropology, University College, London; k.homewood@ucl.ac.uk. Pastoral disease risk management Household and focus group studies of livelihoods and pastoral risk management. Technical report

21. Based on the evidence in the studies listed above, for each country detail how the poor have benefited from the application and/or adoption of the output(s) (max. 500 words):

Input required

- What positive impacts on livelihoods have been recorded and over what time period have these impacts been observed? These impacts should be recorded against the capital assets (human, social, natural, physical and, financial) of the livelihoods framework;
- For whom i.e. which type of person (gender, poverty group (see glossary for definitions) has there been a positive impact;
- Indicate the number of people who have realised a positive impact on their livelihood;
- Using whatever appropriate indicator was used detail what was the average percentage increase recorded

Environmental Impact
H. Environmental impact

24. What are the direct and indirect environmental benefits related to the output(s) and their outcome(s)? (max 300 words)

This could include direct benefits from the application of the technology or policy action with local governments or multinational agencies to create environmentally sound policies or programmes. Any supporting and appropriate evidence can be provided in the form of an annex.

Environmental impacts of the use of vaccines for ECF control compared with the more conventional use of acaricides have been reviewed. The major direct environmental impact of widespread vaccine use will be positive with a reduction in the production, use and disposal of these toxic chemicals. Indirect effects on cattle populations in different production systems are less easy to predict. Reduced mortality risk in young stock will allow livestock keepers more choices and income opportunities but could result in overstocking in some circumstances. However, with significant reductions in calf mortality overstocking to counteract losses due to ECF could be kept to a minimum. Introduction of improved cattle breeds is made possible as demonstrated in northern Tanzania. This could permit greater output of milk and meat from fewer cattle, with a consequent reduction of environmental effects.

Formal bio-safety procedures for assessing the potential environmental impact of deployment of a recombinant vaccine will be conducted prior to and during field trials through the Kenya National Bio-safety Committee. Merial PLC has a number of commercial vaccines deployed worldwide that use the canary and fowl pox virus delivery systems being evaluated for ECF.

25. Are there any adverse environmental impacts related to the output(s) and their outcome(s)? (max 100 words)

Input required? – There has been a fear that with increased survival of ITM-immunised calves there would be greater environmental impact of larger numbers of calves being reared. The Tanzanian study indicates that increased calf numbers are counter-balanced by increased take-off of healthier young stock.

26. Do the outputs increase the capacity of poor people to cope with the effects of climate change, reduce the risks of natural disasters and increase their resilience? (max 200 words)

Input required? – The increased income of poor farmers as a result of ITM permits them to invest in materials and goods that will give them some resilience to natural disasters and climate changes.

The study in northern Tanzania indicates that ITM immunised cattle are healthier and put on weight more quickly this will increase the resistance of these cattle to external stresses. As a consequence, poor people will also be able to cope more effectively with these external stresses.