Field Trials of the Capripox/Rinderpest Recombinant Virus

Executive Summary

Diseases caused by capripox viruses affects around 650 million sheep & goats (pox diseases) and 250 million cattle (lumpy skin disease). This constitutes a massive economic burden for many resource- poor farmers in Africa, damaging their livelihoods and ability to increase their income. The current vaccines are expensive and difficult to deliver as they need a sophisticated cold chain.

The purpose of this project was to test a dual capripox/rinderpest virus vaccine that protects cattle against lumpy skin disease and rinderpest and sheep and goats against pox diseases under African conditions.

The specific scientific/technical aims of the project were:

- To assess, under African conditions, the efficacy of the recombinant capripox/rinderpest virus vaccine developed at the Institute of Animal Health, Pirbright, England, in protecting indigenous livestock against rinderpest, peste des petits ruminants, lumpy skin disease and sheep and goat pox.
- To determine the minimum infectious dose in African cattle, sheep and goats.
- To determine the duration of immunity in African cattle, sheep and goats (3 year trial)

Research Activities included three experiments under local conditions at KARI, Muguga, Kenya, East Africa.

This project successfully tested the efficacy of a dual vaccine against rinderpest and lumpy skin disease (LSD) in cattle. The level of full protection was 100% at one month post vaccination but thereafter declined to 50% at 24 months. Whilst the 50% of animals were solidly protected the remaining cattle some were partially protected and only suffered a mild disease from a viral challenge while over 80% of the animals in the control group succumbed to the disease. Parallel trials undertaken with sheep and goats for Peste des petits ruminants (PPR) showed similar results. Twelve months after vaccination these animals were challenged with isolates from the Ivory Coast. Over 90% of the animals with no previous exposure to capripox virus and 62% with previous exposure were protected. In contrast 90% of the unvaccinated animals showed disease symptoms.

The recombinant vaccine was found to be more thermostable than the conventional tissue culture attenuated vaccine for rinderpest so making it potentially cost-effective in remote areas where it could be used for emergency ring vaccination in the face of a rinderpest outbreak. This would contribute to improved health of farm livestock since the animals would be protected yet remain serologically distinguishable from those that had been naturally infected with rinderpest.

This project demonstrates clear progress towards the project goal of improving the health status of farm livestock owned by poor livestock keepers in East Africa.
However despite this progress further research is still required as vaccine development is a very long process. In particular there is a need complete the 3 year period of the trial to measure the duration and level of protection to livestock. Ideally work is required on extending the level and duration of protection so that a vaccine can be used not just in disease outbreak situations but also in a prophylactic manner. DFID has subsequently funded a number of addition research project to address this matter.

**Background**

Diseases caused by capripox viruses affects around 650 million sheep & goats (pox diseases) and 250 million cattle (lumpy skin disease). Many animals die and the productivity of those that survive is severely reduced. Although Rinderpest has been largely eradicated from many countries it is still endemic in southern Sudan, Ethiopia, Northern Kenya and Uganda and is still a problem in the north of India and Pakistan. Peste des petits ruminants (PPR), blue tongue and foot-and-mouth diseases are still major problems for farmers in many developing countries, especially in East Africa and especially for poor stock keepers.

A recombinant vaccine based on capripox virus expressing the fusion protein gene of rinderpest virus has been produced and successfully tested in experimental animal disease containment facilities at the Institute of Animal Health, Pirbright, UK as part of a previous DFID-funded project. This has been shown to protect cattle from challenge with virulent rinderpest and lumpy skin disease viruses. Such a recombinant virus vaccine has the proven thermal stability characteristic of poxviruses (overcoming the problems of break-down of cold chains) as well as protecting against several important diseases of livestock such as PPR. Being a bivalent vaccine for a particular species the recombinant would also have the practical and economic advantage of controlling with a single inoculation two diseases in each of the target species.

The new vaccine is a modified bivalent capripox-rinderpest recombinant vaccine with that of the original recombinant vaccine which had used a vaccinia late promoter (p11) to drive expression of the rinderpest genes. It was postulated that expression of the rinderpest proteins early in the infectious cycle might enhance the cell-mediated arm of the immune response and improve the effectiveness of the vaccine. An earlier trial had shown that the capripox recombinant produced using the late promoter could protect a proportion of vaccinated cattle for up to three years following a single shot vaccination. However, some vaccinated cattle developed a mild form of the disease and a small proportion succumbed to infection.

**Project Purpose**

The purpose of this project was to test a dual *capripox/rinderpest* virus vaccine that protects cattle against lumpy skin disease and rinderpest and sheep and goats against pox diseases under African conditions.

The scientific/technical aims of the project were:
To assess the efficacy of the recombinant *capripox/rinderpest* virus vaccine under African conditions, in protecting indigenous livestock against rinderpest, peste des petits ruminants, lumpy skin disease and sheep and goat pox.

The importance of this work lies in that the successful testing of a modified recombinant vaccine could lead to its use in potentially controlling, and possibly eliminating economically damaging diseases such as rinderpest and lumpy skin disease from countries like Kenya. An advantage of using recombinant vaccines rather than the conventional tissue culture attenuated vaccine (TCRV) to protect against rinderpest is the ability to distinguish vaccinated animals from those that had recovered from a natural rinderpest infection. This would greatly aid serological surveys and allow the detection of disease circulating in a vaccinated population.

- To determine the minimum infectious dose in African cattle, sheep and goats.
- To determine the duration of immunity in African cattle, sheep and goats (3 year trial)

The experiments also sought to compare the efficacy of the recombinant vaccine with that of the conventional tissue culture attenuated vaccine.

**Research Activities**

Research Activities included three experiments under local conditions at KARI, Muguga, Kenya, East Africa.

**Field Trial 1 - Immunising Dose**

To establish the minimum immunising dose this experiment involved 4 groups of 4 vaccinated cattle, each group receiving a different dose from $10^6$ to $10^3$ pfu and 2 groups of 4 unvaccinated "in contact" control animals. One group of "in contact" animals and all 4 groups of vaccinated animals were challenged with the virulent Kabete O strain of RPV four weeks after vaccination. Three weeks later, the second group of "in contact" animals and recovered cattle from the RP-challenged vaccinated groups were be challenged with virulent LSDV. The animal experiments covered a nine week period and the serology a further six weeks. An exactly parallel trial was set up to assess the minimum infectious dose in African sheep and goats using sheep and goat pox and PPR challenges.

**Field trial 2 - Efficacy**

The protective immunity induced so far by any recombinant vaccine based on a poxvirus, including the recombinant *capripox/rinderpest* virus, has only previously been tested over a short period. Protection afforded by the conventional RBOK rinderpest vaccine is "life-long". Thus, to be acceptable, vaccination with a recombinant Virus must provide immunity of comparable length. It is also necessary that protection given to animals, already immune to LSD at the time of vaccination, is of comparable degree and length.

From a practical and economic point of view, such a field trial needs to be conducted under African conditions with the animals being kept for several years.
Using the effective vaccine dose determined from the results of trial 1 (above) four groups of animals were set up to enable challenges to be performed at 6, 12, 24 and 36 months. Each group consisted of 30 animals, 20 of which were vaccinated and 10 unvaccinated "in contact" controls. Of the 20 vaccinated animals, 15 were confirmed free of antibodies to LSD and five were positive for antibodies to LSD. At the allotted time of challenge, 10 vaccinated but previously LSD negative animals, the 5 vaccinated but previously LSD positive animals and 5 "in contact" control animals were challenged with the virulent Kabete O strain of rinderpest and 5 vaccinated LSD negative and 5 "in contact" control animals were challenged with a lumpy skin disease virus.

Two equivalent trials were set up to assess the efficacy of the vaccine and duration of immunity in both sheep and goats in protecting against challenge with PPRV and sheep and goat pox virus.

Field trial 3 Vaccine stability
One of the major problems associated with the present rinderpest vaccines are their thermolability and shelf life. The development of a recombinant rinderpest vaccine based on capripoxvirus should overcome this problem and this trial tested this. Recombinant capripoxvirus-rinderpest vaccine of the same batch used for trials 1 and 2 was kept under standard conditions in Kenya. At 6, 12, 24 and 36 months samples were used to vaccinate 4 cattle with two additional non-vaccinated cattle being kept as "in contact" control animals. All six animals were challenged with the virulent Kabete O strain of RPV six weeks post vaccination. Analogous experiments were done in sheep and goats.

Outputs
This project successfully tested the efficacy of a dual vaccine against rinderpest and lumpy skin disease (LSD) in cattle and against Peste des petits ruminants (PPR) in sheep and goats. Results from the trials in Kenya showed good short-term protection for vaccinated cattle, and sheep and goats when challenged with lethal rinderpest and PPR respectively. The level of full protection was 100% at one month post vaccination but thereafter declined to 50% at 6, 12 and 24 months. Whilst the 50% of animals were solidly protected the remaining cattle were partially protected and only suffered a mild disease from a viral challenge while over 80% of the animals in the control group succumbed to the disease.

The parallel trials undertaken with sheep and goats for Peste des petits ruminants (PPR) showed similar results. Twelve months after vaccination these animals were challenged with isolates from the Ivory Coast. Over 90% of the animals with no previous exposure to capripox virus and 62% with previous exposure were protected. In contrast 90% of the unvaccinated animals showed disease symptoms.

The recombinant vaccine was found to be more thermostable than the conventional tissue culture attenuated vaccine for rinderpest and it would be cost-effective for use in remote and largely inaccessible areas where the two diseases are prevalent. If the level of protection given by the recombinant vaccine was acceptable to user countries,
then the use of such a vaccine for emergency ring vaccination in the face of a rinderpest outbreak would be beneficial. This would contribute to improved health of farm livestock since the animals would be protected yet remain serologically distinguishable from those that had been naturally infected with rinderpest.

**Contribution of Outputs**

The project goal was to improve the health status of farm livestock. This project demonstrated that the modified form of the recombinant capripox-rinderpest vaccine could protect naïve cattle against a highly virulent Kenyan rinderpest virus and lumpy skin disease for up to two years through inoculation of a single dose of the vaccine. A dual vaccine that can protect cattle against Rinderpest and Lumpy Skin Disease in one vaccination would be of great economic benefit to the livelihood of many poor farmers in areas of the world where these diseases co-exist. The vaccine would also enable animal health workers to distinguish between vaccinated animals and those suffering from Rinderpest. This would be a very useful tool in areas where mass vaccination has been stopped or where civil unrest allowed only intermittent vaccinations or the control of animal movements difficult.

As well as the knowledge gained from this project, undertaking the research at KARI in Kenya has strengthened local research capabilities at both strategic and adaptive levels. KARI staff have gained expertise through the work and on the job training. Links between KARI and IAH have also been strengthened significantly. As this project was undertaken as a collaborative venture between the Institute of Animal Health (IAH) in the UK and the Kenya Agricultural Research Institute (KARI) at Muguga in Kenya the outputs are immediately available to KARI.

The successful development of this type of vaccine will ultimately have a significant positive impact on the livelihoods of subsistence farmers and those dependent on produce such as meat, wool, leather and dairy products from small ruminants. Improved vaccines would make maintaining the good health of livestock easier and cheaper. If this recombinant vaccine fully realises its potential in the next decade then a large market for veterinary vaccines would also be created as demand for such vaccines is very strong.

However despite considerable progress towards a stable field vaccine that could protect livestock belonging to poor farmers in East Africa further research is still required as vaccine development is a very long process. In particular there is a need complete the 3 year period of the trial to measure the duration and level of protection to livestock. Ideally work is required on extending the level and duration of protection so that a vaccine can be used not just in disease outbreak situations but also in a prophylactic manner. DFID subsequently funded a project on these issues R 6557 Field Trialing of the Caprovox/Rinderpest Recombinat Virus that addresses these issues and looked at an improved vaccine.

Work also continued in a series of projects that looked at producing a marked vaccine against rinderpest so that it would be possible to distinguish between vaccinated and infected animals using simple field ELISA tests.
(see DFID funded projects:  
*R7048 Development of a Genetically Marked Rinderpest Vaccine and R7362 Developing a Cheap and Effective Pen-side Test that Differentiated between Vaccinated Animals and those Infected by the Rinderpest Virus*).

**Annex / Appendix**

**Publications:**


**Internal Reports:**

i. 1st Report (Jan 93 - Dec 93) - January 1994  
ii. Quarterly Report - May 1994  
iii. Quarterly Report - August 1994  
v. Quarterly Report - February 1995  
vi. Quarterly Report - May 1995  
ix. Quarterly Report - February 1996  
x. Quarterly Report - May 1996  
xi. Quarterly Report - April 1997

**Other Dissemination of Results.**

i. The work has been presented at two international meetings: PARC technical meeting held in Kenya in April 1998 and the FAO/EMPRES meeting held in Rome in September 1998.  