



Introduction to the study project entitled:

Understanding Rift Valley Fever in the Republic of South Africa Led by:

- National Institute for Communicable Diseases Centre for Emerging and Zoonotic Diseases
- EcoHealth Alliance

The study is an investigation into how Rift Valley fever virus might spread amongst animals and people, how it is maintained in the mosquito vector, animals and/or people, during the time between outbreaks of disease, what effect climate, soil and vegetation may have on the virus and the vector, how the current level of antibodies in people and animals and vaccination strategies may affect the risk and the magnitude of an outbreak in livestock and people.

Results from the study may inform policy decisions and evidence-based practice by identifying risk factors for disease and targets for preventive healthcare and improved disease control.

This will be the first long-term study to investigate Rift Valley fever (RVF) virus simultaneously in people and domestic and wild ruminants.

The Centre for Emerging and Zoonotic Diseases and EcoHealth Alliance are implementing surveys during 2015 – 2019 to understand the spread of mosquito borne diseases to farmed animals and the spread of diseases from farmed animals to people in the Free State and Northern Cape. Surveys will include assessments of short- and long-lived antibody titers against RVF virus in people and ruminants (livestock and farmed and wild animals) in the study area depicted below.

This study is approved by the Witwatersrand University Human Ethics Committee (HHREC M140306) and University of Pretoria Animal Ethics Committee (t008-14).



Location of the study area in the Free State and parts of the Northern Cape





The RVF Survey in people, livestock and farmed game 2015 - 2019:

Disease exposure evaluation of animals and people through determination of anti-RVF virus antibody levels

Local Stakeholder Meeting:

We will host an annual local stakeholder meeting for farmers, farm workers and other people working with animals (e.g. veterinarians, abattoir personnel) and living within the study region to initially introduce and then annually update the project. A summary of the results will be reported each year at these meetings and as requested by local farmers' unions.

Antibody determination in animals:

Study 1: Ruminant Cross-Sectional Study:

We will conduct a large-scale metapopulation survey for RVF antibodies of **farmed wildlife**, **domestic livestock** and **free-ranging wildlife**. Up to three species of **domestic livestock** (cattle, sheep and goats), three species of **farmed game** (springbok, blesbok and kudu) and four species of **free-ranging wildlife** (buffalo, springbok, kudu and wildebeest) within the study area will be appropriately handled for blood specimen collection. Farms will be included based on random selection so as to include a representative sample of at risk animals in the study area. The cross-sectional study will be conducted across the region during two separate years.

Blood specimens collected from animals will be tested for short- and long-lived RVF virus antibodies using specialised standardised tests for wildlife to indicate the overall state of prevalence of RVF virus exposure in animals in the study area.

The cross-sectional study will give an overall population level picture of the exposure risk in animals that are at risk for disease within the study area.

Study 2: Sheep Cohort Study

We will also follow a cohort of animals (sheep only) over time to investigate how antibody levels against RVF virus change over time in sheep.

Through the local stakeholder's meetings or identified from the ruminant cross-sectional study 1, we will recruit interested **sheep** farmers to voluntarily enroll their animals in the study.

The study sheep will be randomly assigned to one of up to four study groups, based on pre-determined antibody levels. Seronegative animals (no previous exposure) will receive one of the following treatments: modified live vaccine and/or inactivated vaccine and no vaccine. A seropositive (previous exposure) group will constitute the control group.

Farmers will manage the study animals in the usual animal management practices on the farm, with the exception that the study **animals must remain in the study for 4 years**. Farmers will be compensated for not selling/slaughtering their stock to remain in the study.

Study animals will be identified (ear tags, tattoos or microchips) and may be vaccinated with commercially available vaccine at the start of the study as outlined above. Every 3 months thereafter, a blood specimen will be collected from each animal for the duration of the study (4 years).

Blood specimens will be tested for short- and long-lived antibody titres against RVF virus using specialised, standardised testing methods. Participant farmers will be encouraged to report ANY adverse event (e.g. abortion or fever) after the study start in the study animals so the study veterinarian can determine the cause of the adverse event.





Antibody determination in people:

In this part of the study, **people** in the study area, at high risk of contracting RVF virus infection because they live or work with livestock, will be invited to participate in one of our two studies.

Study 3: Cross-Sectional Study in People (people within the study area that only participate once)

In co-ordination and simultaneously with study 1 above the cross-sectional study in people will give an overall population level picture of the exposure risk of people having frequent contact with animals in the study area. Participants from the general population within the study area will be invited to join. This group of people will allow us to assess the antibody level against RVF virus in the farming population within the study region. Farms will be included based on random selection so as to include a representative sample of at risk people in the study area. Abattoir workers and veterinary and para-veterinary personnel from the study region will be recruited in the same way to participate in parallel to the farm and farm worker RVF virus surveys.

Participants will be asked to complete a short questionnaire about their contact with animals and potential exposure to RVF and also provide a small blood specimen (collected by a qualified health professional) for RVF virus short- and long-lived antibody testing. Additionally, farm owners and/or managers will be asked to complete a second questionnaire regarding the type of animals they keep on the farm. This group will only be asked to participate once during this study. The exercise will be conducted during two separate years to ensure adequate number of participants from the farm, veterinary and abattoir groups. It is preferable that the people sampled are from the same farms for which we are sampling ruminants as part of study 1in order to estimate actual human risk.

Study 4: Cohort study (a constant group of people followed over time for 4 years)

Using the results of the cross-sectional we will invite farmers/farm workers, veterinarians and abattoirs to participate. Participation is voluntary. Once identified, times will be scheduled to visit farms or homes. Other members of the household or workers at the participant farms will also be invited to participate, making up the cohort group of people in study 4.

The cohort participants will be asked to complete the same questionnaire as given in study 3 and give a small blood sample (collected by a qualified health professional) **on an annual basis for 4 consecutive years**. Each year participants will be given the results of the previous round of testing, unless a current RVF virus infection is detected. In these cases the participant will be notified as soon as the test results are available and will be counseled by an infectious disease expert from NICD and referred to a physician.

Blood specimens collected will be tested for short- and long-lived antibody titres against RVF virus. People with evidence of short-lived RVF virus antibodies (suggestive of possible recent infection) will be requested to give a second blood specimen 4 weeks after the first to estimate period of antibody production, follow up on the recovery process and persistence of antibody levels.

All testing for people and animals will be processed at one of the following laboratories: the National Institute for Communicable Diseases in Johannesburg, Onderstepoort Veterinary Institute in Pretoria or the provincial Department of Agriculture of the Free State and Northern Cape in Bloemfontein and Kimberley respectively.

The results of these studies will be used to determine the levels of previous exposure (antibody titres) to RVF virus in the study area in both people and animals. We will combine the population-level exposure information from the cross sectional studies (1 & 3) with the information on the change of antibody levels over time through the cohort studies sheep and people (2 & 4 respectively). This information may be used to inform national and local policy decisions and evidence-based practice by identifying risk factors for disease and targets for preventive healthcare and improved disease control.