LIVE
RIFT VALLEY FEVER
VACCINE FOR CATTLE, SHEEP AND GOATS

Freeze-dried, live attenuated Rift Valley fever virus (Smithburn strain) for the immunisation of cattle, sheep and goats against Rift Valley fever.

Store the vaccine in a refrigerator at a temperature of 4°C to 8°C. Do not use after the expiry date printed on the bottle.

RECOMMENDATIONS FOR USE
Animals can be vaccinated at any age except that lambs, calves and kids from immune animals should not be inoculated before they are six months old because maternal antibodies may block the vaccine response. This disease occurs during the late summer and autumn and it is therefore best to inoculate susceptible animals during this time, three to six weeks before the mating season. Where possible, breeding should also be deferred so that ewes lamb from February to April to ensure that lambs will be adequately protected by maternal antibodies during the time of the year that this disease occurs. Annual vaccination is recommended.

WARNINGS
Do not slaughter animals for human consumption within 7 days of vaccination. Vaccinate healthy animals only. Keep out of reach of children, untrained persons and animals. Under normal circumstances pregnant animals should not be inoculated with this vaccine as it can cause abortion or foetal malformation. In a small percentage of animals, particularly sheep, although this product has been extensively tested under a large variety of conditions, failure thereof may ensue as a result of a wide range of seasons. If this is suspected, seek veterinary advice and notify the registration holder.

DIRECTIONS FOR USE
Use only as directed.
Sterile syringes and needles by boiling in water for at least 15 minutes. Do not use disinfectants or methylated spirits for sterilising either syringes or needles. The active ingredient of the vaccine is in the form of a powder or pellets. Place 5 ml of water into the bottle containing the freeze-dried vaccine. Mix thoroughly until the powder is dissolved. Transfer the suspension back to the remaining diluent and again mix well. The vaccine is now ready for use and must be injected without delay. Avoid exposure to high temperature and direct sunlight during inoculation. Shake the bottle before filling the syringe. Use a separate needle for each animal, particularly during outbreaks of the disease.

DOSE:
Cattle, sheep and goats: 1 ml subcutaneously

EFFECTS OF THE VACCINE
A slight febrile reaction may occur on the second to fourth day following inoculation but subsides rapidly. Full immunity is usually obtained three weeks after inoculation, but cannot be guaranteed in all animals.

PACKING
Available in bottles of 100 does.

Registration holder:
Onderstepoort Biological Products SOC Ltd, Reg. No. 2000/02/265850/06
Private Bag X007, Onderstepoort, 0110. Tel.: +27 (0) 12 522 1500, Fax: +27 (0) 12 522 1591
Made in South Africa
INACTIVATED
RIFT VALLEY FEVER
VACCINE FOR CATTLE, SHEEP AND GOATS

Formalin inactivated Rift Valley fever virus with aluminium hydroxide gel as adjuvant for the prophylactic immunisation of cattle, sheep and goats against Rift Valley fever.

Store the vaccine at a temperature of 4°C to 8°C, in a refrigerator. Do not use the vaccine after the expiry date printed on the bottle.

RECOMMENDATIONS FOR USE
Susceptible animals can be immunised at any age irrespective of the stage of pregnancy and lactation. Calves and lambs from immune animals can only be effectively immunised after the age of six months. Annual vaccination is recommended and it is advisable to immunise in the late winter or early spring.

WARNINGS
Do not slaughter animals for human consumption within 7 days of vaccination. Vaccinate healthy animals only. Keep out of reach of children, uninformed persons and animals. Although this product has been extensively tested under a large variety of conditions, failure thereof may ensue as a result of a wide range of reasons. If this is suspected, seek veterinary advice and notify the registration holder.

DIRECTIONS FOR USE
Use only as directed.
Sterilise syringes and needles by boiling in water for at least 15 minutes. Do not use disinfectants or methylated spirits for sterilising syringes or needles. Use a separate sterile needle for each animal. Shake the bottle well each time before use. Avoid exposure to high temperatures and direct sunlight.

DOSEAGE:
Cattle: 2 ml subcutaneously
Sheep and goats: 1 ml subcutaneously

EFFECTS OF THE VACCINE
Optimal protection is conferred when a booster is given 3 - 4 weeks after initial vaccination but cannot be guaranteed in all animals. Thereafter vaccinate annually.

PACKING
Available in bottles of 100 ml.

Registration holder:
Onderstepoort Biological Products SOC Ltd, Co. Reg. No. 2000/022686/06
Private Bag X07, Onderstepoort, 0110. Tel: +27 (0) 12 522 1500, Fax: +27 (0) 12 522 1591

Made in South Africa
RVF CLONE 13
VACCINE FOR CATTLE, SHEEP AND GOATS


100 ml

DOSE:
Cattle, Sheep and Goats: 1 ml subcutaneously

Storage: 4°C - 8°C See package insert for full instructions.

REFERENCES:
For animal use only.

FREEZE-DRYED, LIVE ATTENUATED Rift Valley Fever Virus (Clone 13 strain) for the immunisation of cattle, sheep and goats against Rift Valley Fever.

Store the vaccine at a temperature of 4°C to 8°C in a refrigerator. Do not use the vaccine after the expiry date printed on the bottle.

RECOMMENDATIONS FOR USE
Rift Valley Fever is a mosquito-borne disease which occurs sporadically in South Africa especially during seasons of high rainfall. During outbreaks, the disease is prevalent in late summer to autumn (February - March). Animals should therefore be immunised in early summer to prevent infection. Young animals can be immunised with safety from 2 months of age, unless their mothers were vaccinated in which case they should be vaccinated at 6 months of age. The vaccine has been shown to be safe for use in pregnant animals. Vaccinate animals annually to ensure optimal immunity.

WARNINGS
Do not slaughter animals for human consumption within 21 days of vaccination. Vaccinate healthy animals only. Keep out of reach of children, uninform people and animals. Safe for use in pregnant animals. Although this product has been extensively tested under a large variety of conditions, failure thereof may occur as a result of a wide range of reasons. If this is suspected, seek veterinary advice and notify the registration holder.

DIRECTIONS FOR USE
Use only as directed.
Sterile syringes and needles by boiling in water for at least 15 minutes. Do not use disinfectants or methylated spirits for sterilising either needles or syringes. The active ingredient of the vaccine is in the form of powder or pellet in a small bottle. By means of a sterile syringe, transfer 0.5 ml of the vaccine into the bottle containing freeze-dried vaccine. Mix thoroughly until the powder is dissolved. Transfer the suspension back to the remaining diluent and again mix well. The vaccine is now ready for use and it must be injected without delay. Avoid exposure to high temperatures and direct sunlight. Shake the bottle before filling the syringe. Use a separate needle for each animal, particularly during outbreaks of the disease. After re-suspension of the vaccine, animals should be vaccinated within 2 hours.

DOSE:
Cattle, Sheep and Goats: 1 ml subcutaneously

EFFECTS OF THE VACCINE
A slight febrile reaction may occur on the second to fourth day following inoculation but subsides rapidly. Most animals will be immune three weeks after vaccination, although this cannot be guaranteed. Annual vaccination is recommended.

PACKING
Available in bottles of 100 doses.

Registration holder:
Onderstepoort Biological Products (Ltd), Co. Reg. No. 2000/022686/06
Private Bag X07, Onderstepoort, 0110, Tel: +27 (0) 12 522 1500,
Fax: +27 (0) 12 522 1591

Made in South Africa.

Lunar Printers.
Smithburn RVF vaccine – Smithburn neurotropic strain (SNS - neuroadapted). Developed in 1949 via i.c. passages (~102)of the pathogenic Entebbe strain in mice


MLV further developed via amplification of SNS in BHK-21 cells – distributed to several countries including 22 m.d. in Namibia and SA from 1974 to 1976; 4.2 m. d. in SA Israel, and Egypt in 1977, 3 m.d. in Zimbabwe from 1978-1979, and ~ 10 m.d. in Saudi Arabia in 2001.

Since 2010, the **Clone 13 vaccine** (69% in-frame truncation of the NSs gene, which is a major virulence factor for RVFV) has been registered in SA, Namibia, Botswana, Zambia and Mozambique.

A second RVF Clone 13 vaccine, **thermostable Clone 13 vaccine** (Clone 13T vaccine), has been developed and registered in Morocco by MCI Sante Animale. Generated via selection of viable virus at 56°C from the culture supernatant of Vero cells and then lyophilized in the presence of a stabilizer. Also used in Senegal and Mali.
Results of recent genetic analysis indicate that natural history of RVFV might be influenced by massive vaccination with SNS vaccine.

Millions of doses were administered to livestock, particular sheep, at times when the virulent RVFV was actively circulating in the animal population.

Multi-doses vials commonly administered with automatic syringes while needles not change often enough.

Viruses passaged (attenuated) by intracranial inoculation of mice may acquire new tissue tropism and pathogenic properties.

Genetic footprint of SNS exists in many RVF linages (vaccine lineages).
<table>
<thead>
<tr>
<th>Type of Vaccine</th>
<th>Host Species Evaluated/Used in</th>
<th>DIVA</th>
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<tbody>
<tr>
<td></td>
<td>Mice</td>
<td>Sheep</td>
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<tr>
<td>Inactivated</td>
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<td>√</td>
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<tr>
<td>NDBR103</td>
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<tr>
<td>TSI GSD 200</td>
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<td>Formalin Inactivated (South Africa)</td>
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<td>Formalin inactivated (Egypt)</td>
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<tr>
<td>Genetically non-modified-live</td>
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<tr>
<td>Smithburn</td>
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<tr>
<td>MP12</td>
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<tr>
<td>Genetically modified-live</td>
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<td>Clone 13, CI13T</td>
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<td>R566</td>
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<tr>
<td>Recombinant MP12 Δ/mutants</td>
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<tr>
<td>Recombinant ZH501 Δ/mutants</td>
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<td>Four-segmented RVFV</td>
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<td>Recombinant protein vaccines</td>
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<tr>
<td>DNA vaccines</td>
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<td>Virus-like particles (VLPs)</td>
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<td>Virus replicons</td>
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<tr>
<td>Modified vaccinia Ankara</td>
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<tr>
<td>Equine herpesvirus virus type 1</td>
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</table>

a = Human volunteers; b = goats and camels; NHP = non-human primates.

Faburay B et al. Vaccines 2017