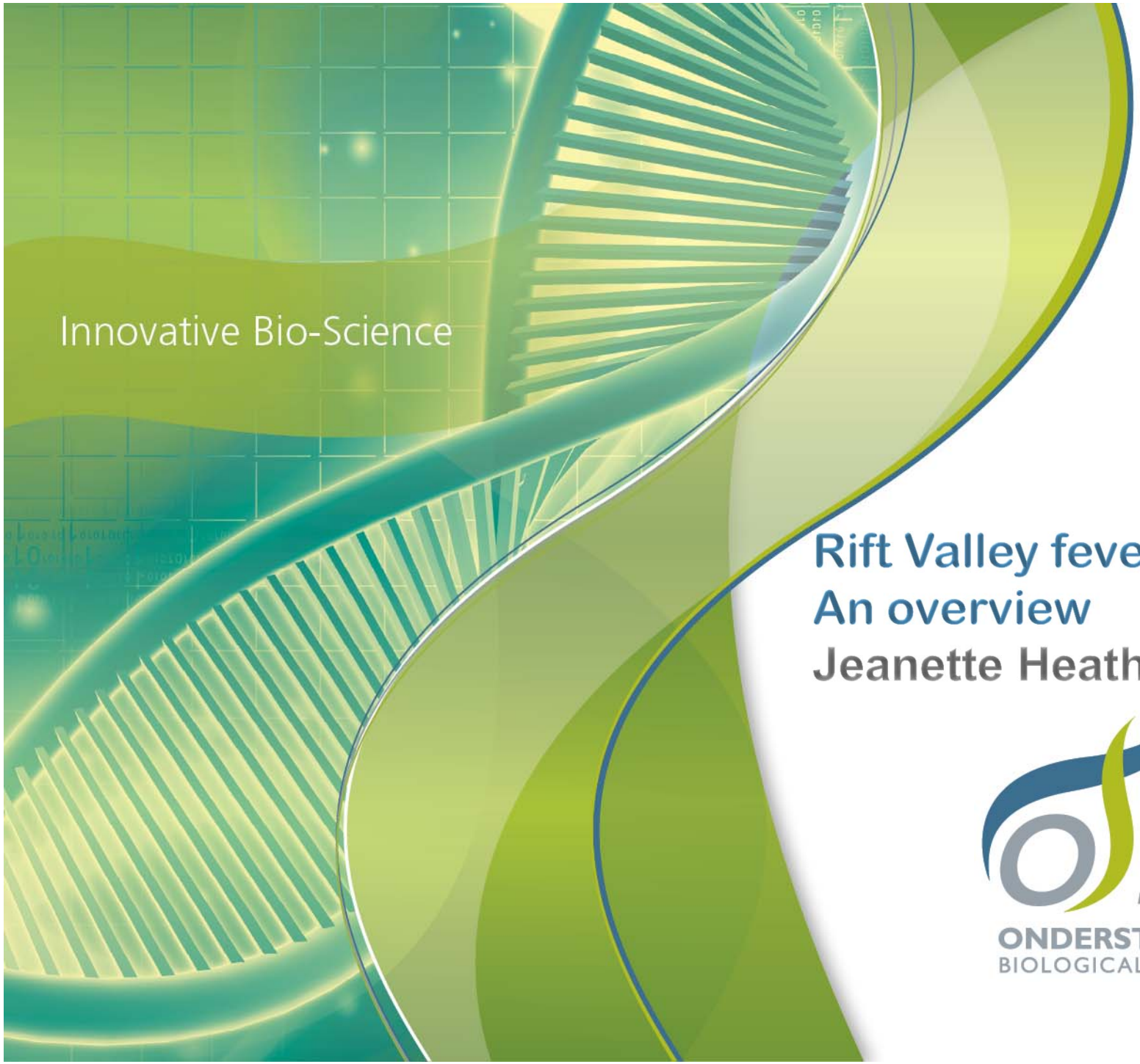


# Rift Valley fever vaccines: An overview

Jeanette Heath

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# Presentation Outline

- Commercial RVF vaccines
  - “Old” – Smithburn, inactivated
  - “New” – Clone 13
- RVF Clone 13 performance in the field
- Candidate RVF vaccines in the pipeline

# Commercial RVF vaccines

**Inactivated vaccine (virulent field strain) (1977)**

- Wild-type, virulent virus
- Inactivated adjuvanted vaccine
- Long lead time
- High antigen payload required
- Safe in pregnant animals
- Can be used in outbreak
- Booster dose and more frequent vaccination required to maintain adequate level of immunity

Concerns:

- Special, isolated production facility needed – occupational hazard/risk
- Perform poorly in controlling epizootics

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# Commercial RVF vaccines

**Live attenuated (Smithburn strain) (1971)**

- Mouse adapted partially attenuated
- Smithburn strain
- Easy and safe to produce
- Cost effective production
- Relatively short lead time
- Immunogenic after single dose
- Long lasting immunity but recommend vaccination annually in endemic areas

Concerns:

- May be teratogenic in pregnant sheep
- Risk of reversion to virulence
- Not advisable for use in an outbreak

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# Commercial RVF vaccines

**RVF Clone 13**
**(August 2010, South Africa & Namibia)**

- Live, naturally attenuated vaccine, isolated from a benign human case
- Easy and safe to manufacture
- Cost effective production
- Relatively short lead time
- Immunogenic after single dose
- Long lasting immunity but recommend vaccination annually in endemic areas

Advantages:

- Absence of virulence
- Safe for use in sheep, goats and cattle irrespective of pregnancy status

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Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine


# Safety and efficacy of Rift Valley fever Smithburn and Clone 13 vaccines in calves

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[d] Institut Pasteur, Unité de Génétique Moléculaire des Bunyavirus, 75724 Paris, Cedex 15, France

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine


# Evaluation of the efficacy and safety of the Rift Valley Fever Clone 13 vaccine in sheep

Baptiste Dungu[a,*], Ian Louw[a,1], Alison Lubisi[b,2], Pamela Hunter[a,3], Beate F. von Teichman[a,4], Michele Bouloy[c,5]

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# RVF Clone 13 field trials

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# Cattle trial (Heilbron)

- 12 cattle owners in the Free State, Heilbron district
- >20 000 cattle
- Different breeds (e.g. Bonsmara, Limosin, Angus, Holstein, Drakensberg)
- All ages (incl. 0-4 months, 4-6 months)
- All stages of pregnancy
- Vaccination with Clone 13 Feb/March 2010
- RVF outbreak started end of March 2010
- No complaints (owner/vet) post-vaccination
- No abortions reported post-challenge

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# Sheep trial (Merino consortium)

- Victoria-Wes, Northern Cape Province
- Young breeding ewes
- 3 flocks on separate farms
- **Aim**: determine antibody response in vaccinated sheep over a period of 12 months

- RVF Clone 13 (batch 9)
  - 1ml, subcutaneous
  - 2 farms, total of 547 ewes
- RVF Smithburn (Batch 110)
  - 1ml, subcutaneous
  - 1 Farm, 180 ewes

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# Sheep trial (Merino consortium)

- Sero-conversion was confirmed with ELISA (ARC-OVI) & SNT
- D28 pv – ≥95% sero-conversion
- Maternal Ab in lambs born from vaccinated ewes were corresponded to high Ab titres of ewes (SNT titres 1:16 to ≥1:512)

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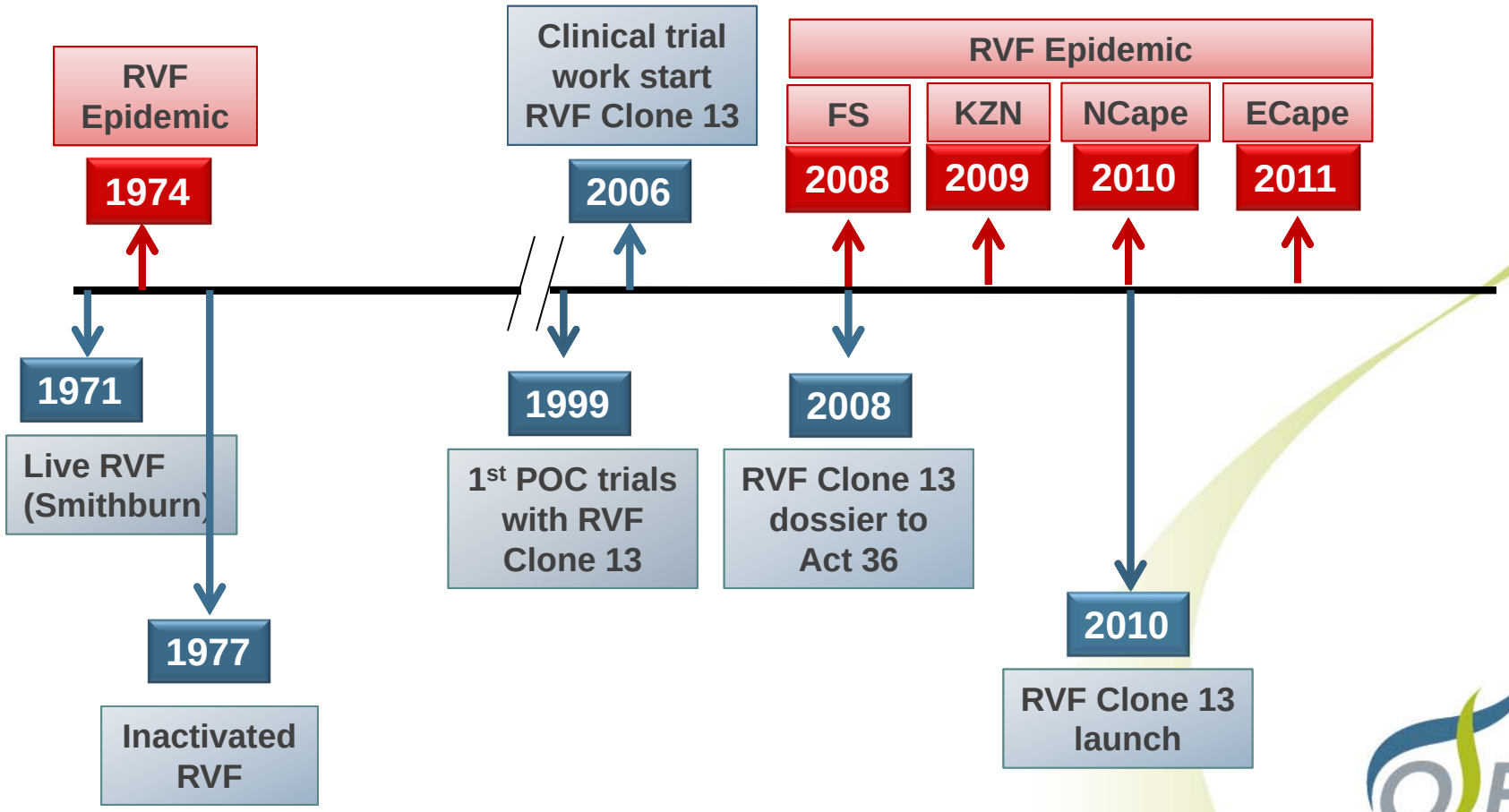
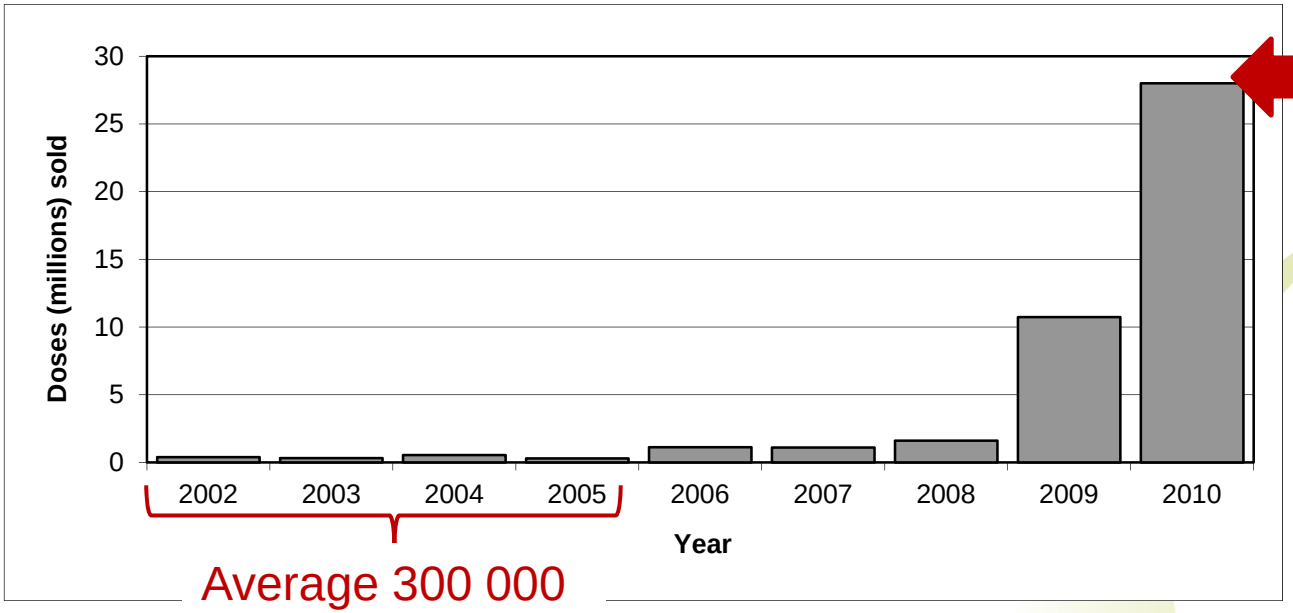
# RVF timeline



# Onderstepoort RVF vaccines

## Situation in South Africa

- during outbreaks a huge demand for vaccines (1973/74; 1994; 2008/09; 2010)
- In between outbreaks – vaccine stock often destroyed due to expiry




OBP RVF vaccine doses sold in South Africa between 2002 and 2010.

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# Customer complaints

- OBP RVF vaccines in use >50 years
- Most of this in endemic areas, outside SA
- No adverse reactions reported

- Period April 2010 – March 2011: 28 million RVF doses sold – 38 customer complaints received

- Mainly from the Aberdeen/Graaff-Reinet area (central Eastern Cape province.
  - 50:50 Live RVF:RVF Clone 13

# Customer complaints

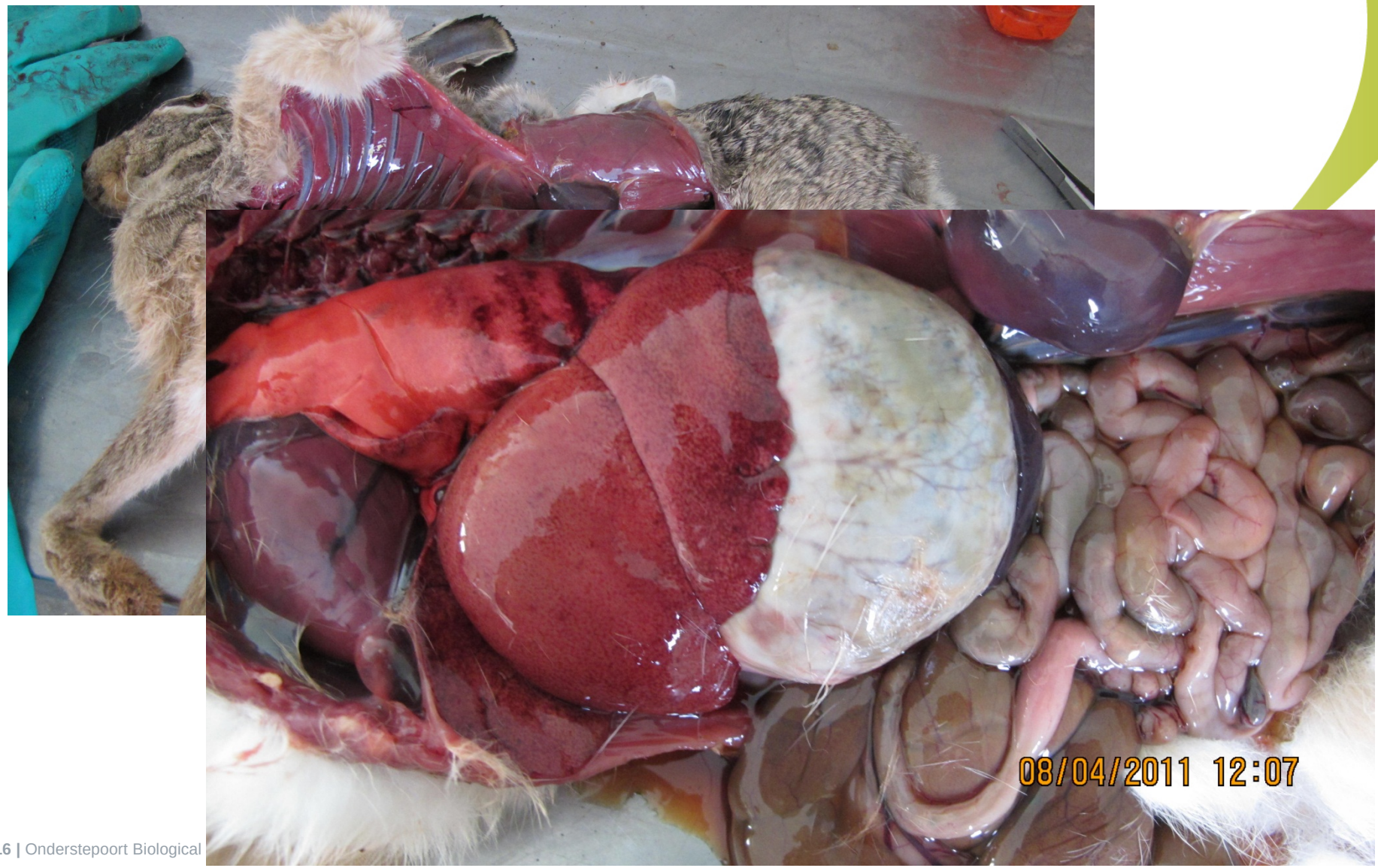
- Articles (Landbouweekblad & Farmers weekly) focused a lot of public attention on apparent vaccine failures
  - Cold chain not maintained
  - Vaccine not effective

- Launched an investigation into the alleged ineffectiveness of our RVF vaccines
  - Visited customers
  - Questionnaire
  - Visited state and local veterinarians

# What did we find?

- Worst draught in 100 years” followed by 200% - 400% annual rain fall
  - No vaccination up to 2009
- Massive insect load

# What did we find?



# What did we find?

- All insect borne viruses present – massive antibody titres
  - Wesselsbron virus
  - Bluetongue virus
  - Some West Nile virus
  - [Some Chlamydia (Enzootic abortion)]

- Not a cold chain problem

# Prof Bob Swanepoel

"I think the large scale use of Clone 13 after the subsidence of the outbreak/mosquito activity in the 2nd half of 2010 represents a significant break with history …. Vaccination on that scale during a relatively quiescent period during a time of RVF activity is a breakthrough and I think we were all surprised at how relatively little virus activity occurred in 2011 (despite good rains) in the areas most severely affected in 2010 and where presumably most vaccinating was done … I think this is more of a triumph for timely and significant scale usage of vaccine possibly for the first time ever."

# New candidate RVF vaccines in the pipeline

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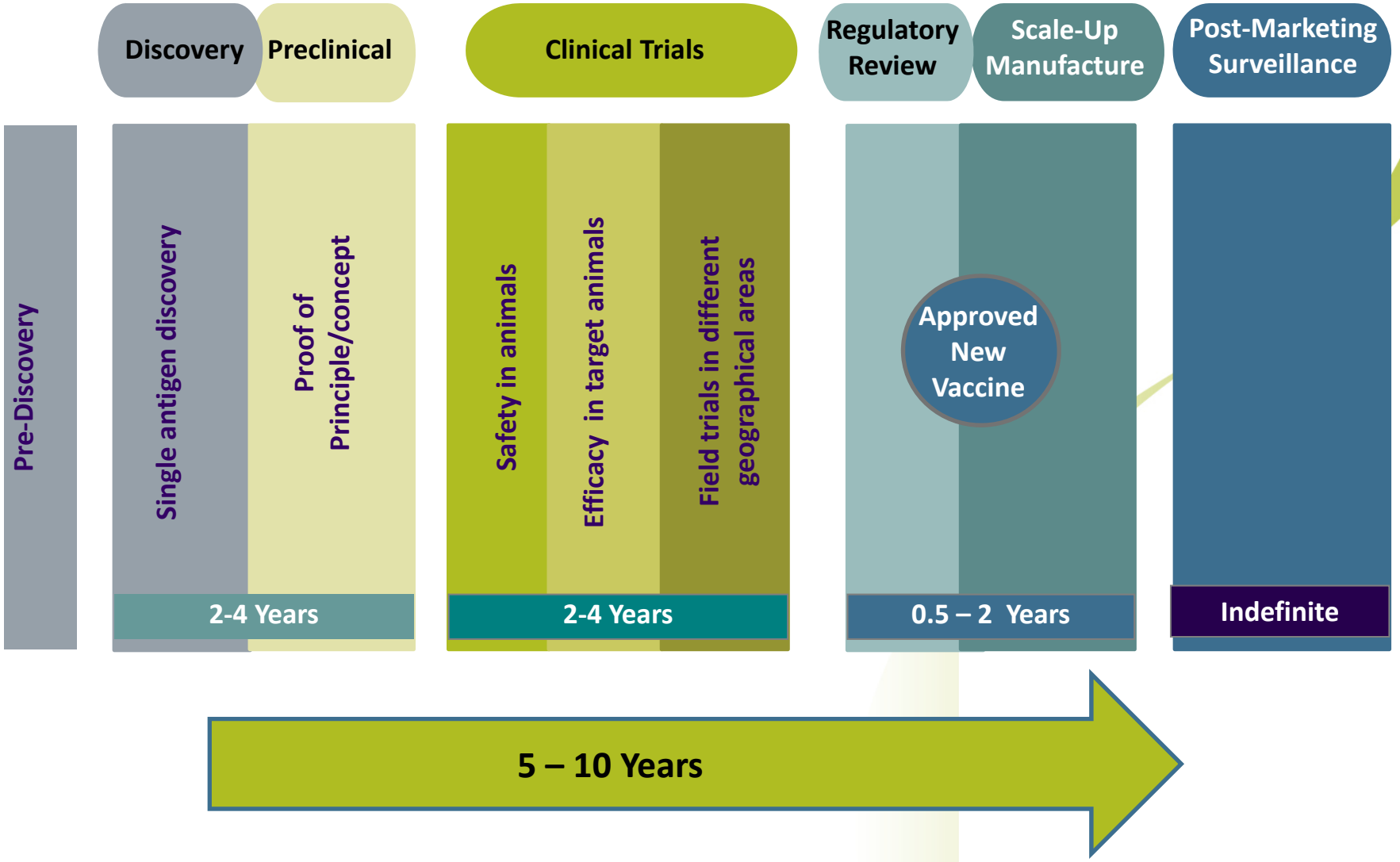
# Vaccine Development



# Candidate RVF vaccines

- MP-12
  - Human isolate, attenuated by serial passage in presence of a mutagen
  - Mutation on all 3 genomic segments
  - Immunogenic, safe in pregnant animals
  - Sheep, cattle and human
  - DIVA possible
- ΔNSm/ΔNSm RVFV
  - Reverse genetically produced
  - Studies in rats and sheep
  - DIVA possible
- Viral vectors
  - Lumpy skin disease virus
    - Live, attenuated LSD virus expressing RVF G proteins
    - Tested in sheep
  - Newcastle Disease virus
    - NDV expressing RVF Gn and Gc glycoproteins
    - Booster needed
    - Tested in calves & sheep

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