New developments in Rift Valley fever vaccination

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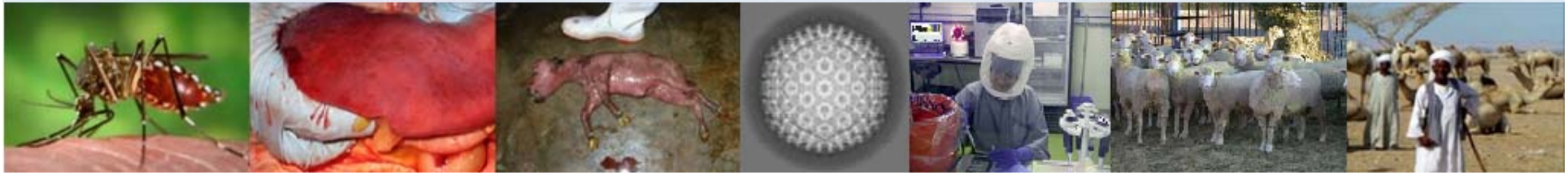
Djibouti



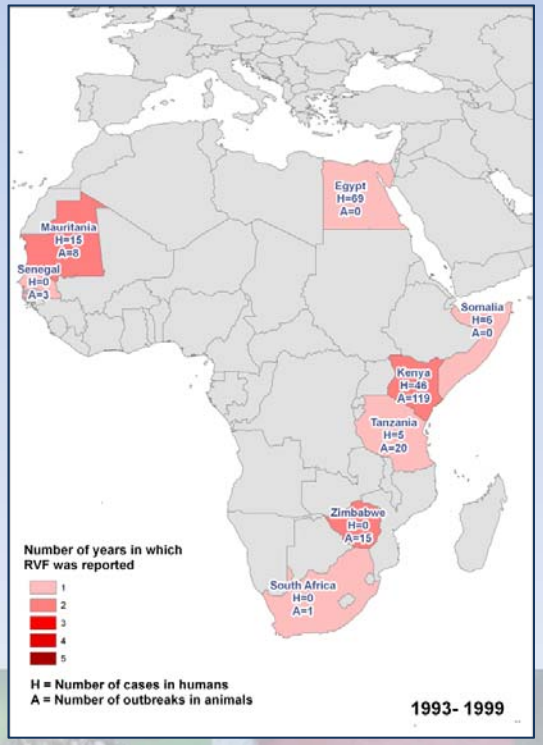
RVF vaccination

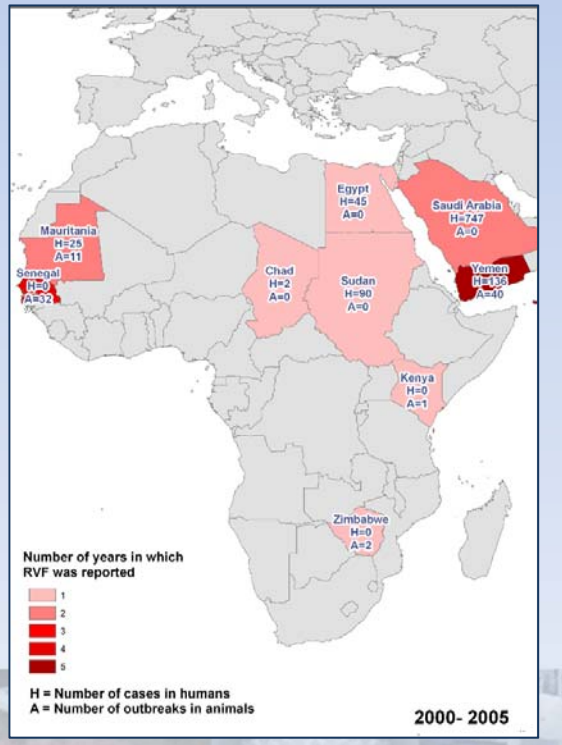
Current live attenuated and inactivated vaccines are effective!

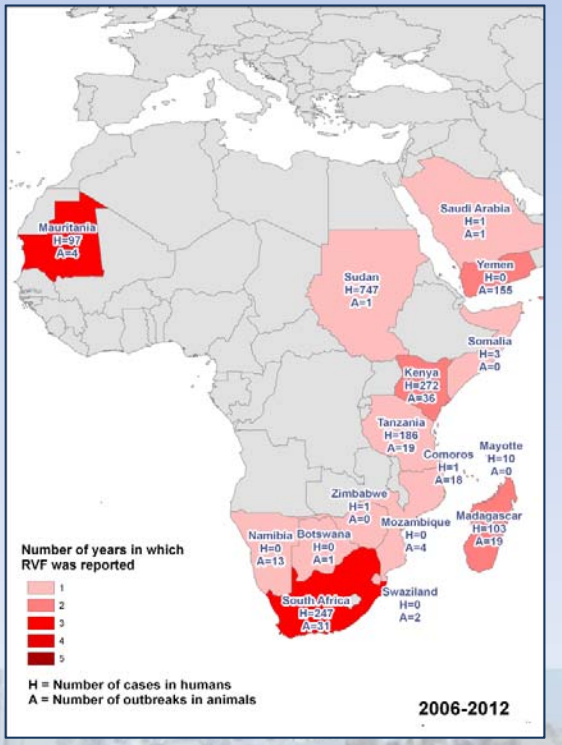
So why do we work on new vaccines?

Rift Valley fever vaccination

- How effective is our current control strategy?

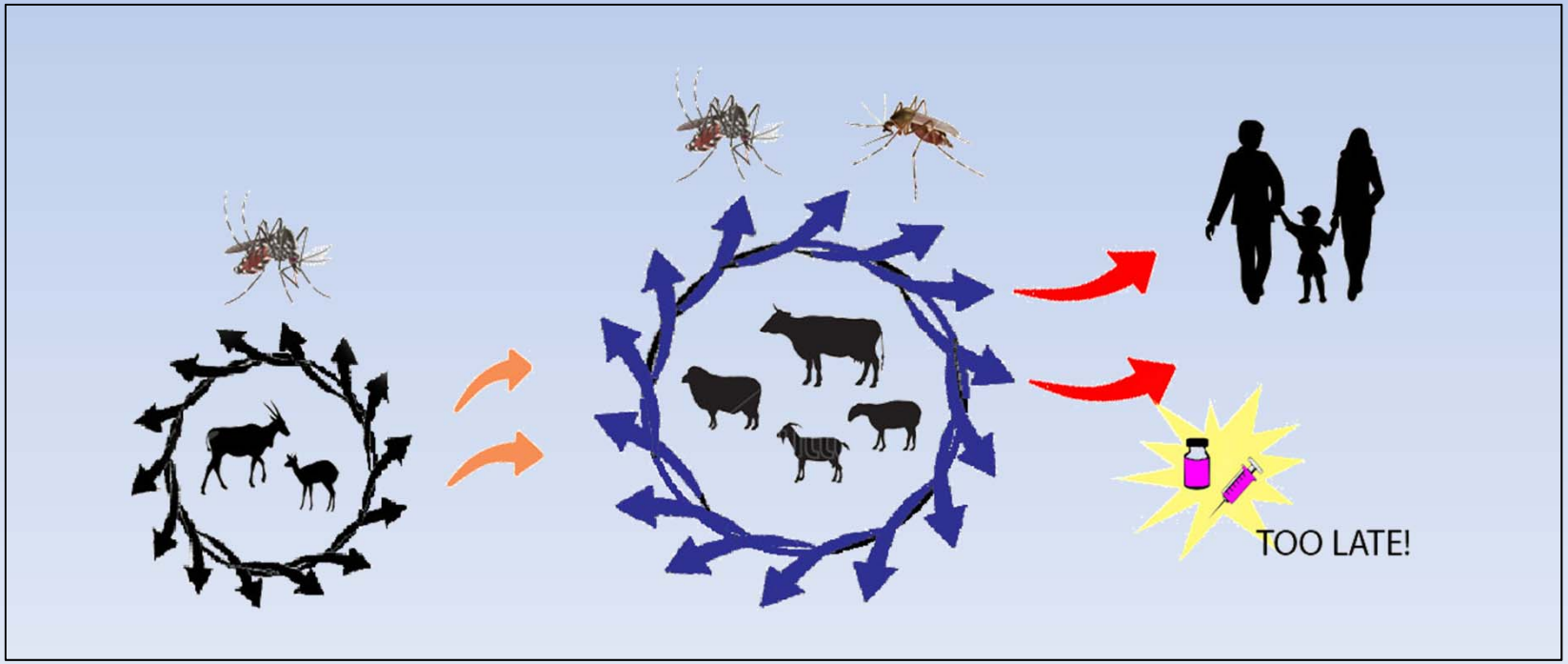






1993-1999 2000-2005 2006-2012

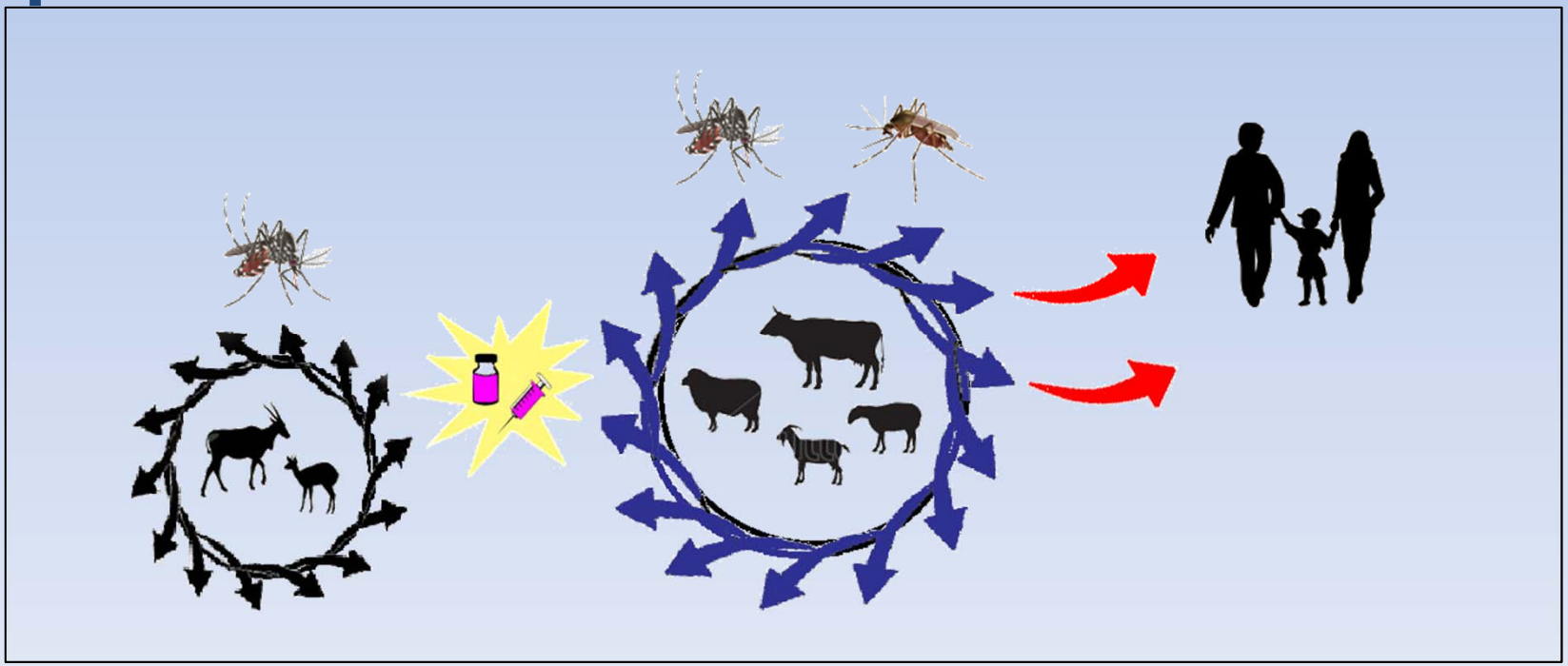
Late detection → late vaccination → cannot stop RVF outbreaks



Enzootic cycle → Epizootic cycle → Spill-over zoonotic disease

DELTAMUNE

Timeous / routine vaccination → prevents epizootic cycle → prevents spill-over in humans



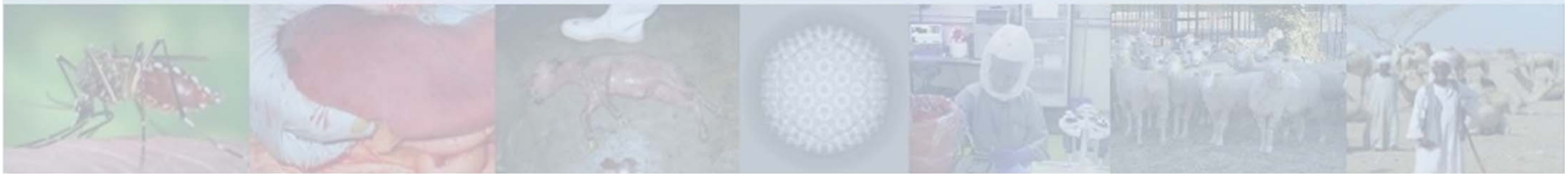
Enzootic cycle → Epizootic cycle → Spill-over zoonotic disease

DELTAMUNE

ROUTINE VACCINATION!

<u>Need new generation vaccines with:</u>

- **Improved safety** (pregnant animals)
- Equivalent or improved efficacy
- Cost effective
- DIVA will be an advantage



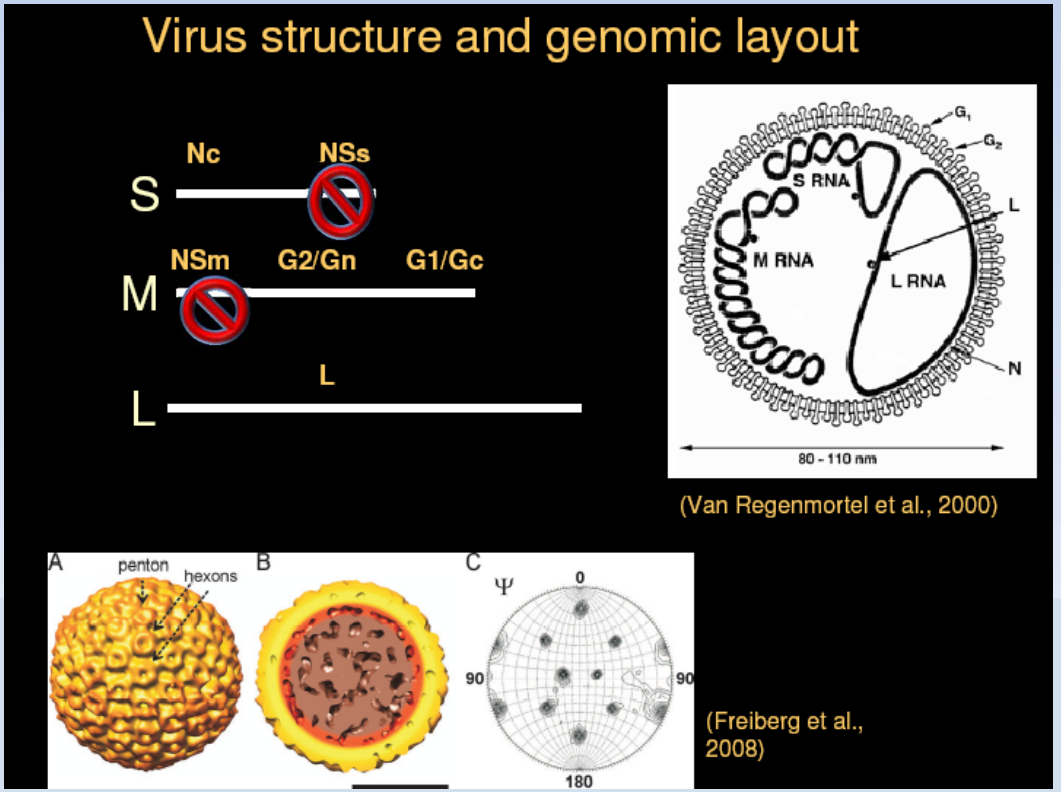
New vaccine candidates

- **Live vaccines:**
  - Reassortants (e.g. R566)
  - Reverse genetics vaccines (rZH501: ΔNSsΔNSm, MP12: NSm
  - Vector vaccines (NDV/GnGc, LSDV/GnGc, MVA/M4, MVA/N)
  - DNA vaccines (pCMV-M4, PCMV-N, Gn-C3d-DNA, Gn-DNA)
  - Replicons (iVLPs)

- **Inactivated vaccines:**
  - Subunit vaccines (GnGc VLPs, GnGc-N VLPs, GnGc/MoLV chimeric VLPs)

Reverse genetics RVF vaccine

- RVF virus deleted virulence factors, NSs and NSm (DDvax)
- Developed by CDC
- Evaluated by Deltamune



Bird et al. 2008, 2010

DDvax: Safety features

- Similar to Clone 13, but
  - lower potential for reassortment
  - negligible potential for insect transmission

- Very little side effects:

	10^4	10^5	10^6
– Clinical	0	0	0
– Viraemia	0	0	0
– “RNA-aemia”	31%	0	30%
– Abortion	0	0	0
– Teratology	0	0	10%

- Safety trials in goats in progress

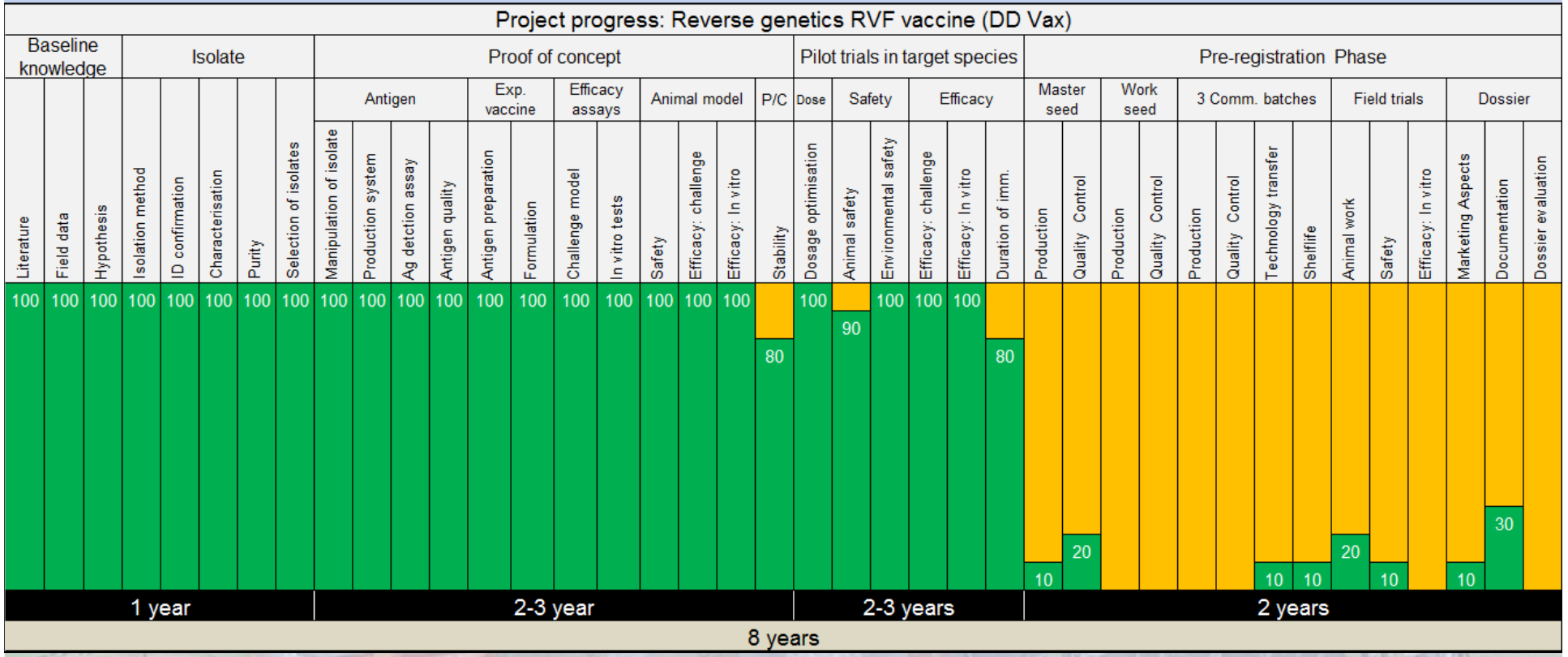
DDvax: Vaccine efficacy

- Single vaccination: (10^4 – 10^5 $TCID_{50}$)
- Moderate levels Ab^{neut} [rats, sheep, cattle, goats*]
- Protect sheep against:
  - Viraemia: 100%
  - Clinical signs: 100%
  - Abortion – singlet: 100%
  - Abortion – twins: 94%

- Duration of immunity trial in process.

Reverse genetics vaccine

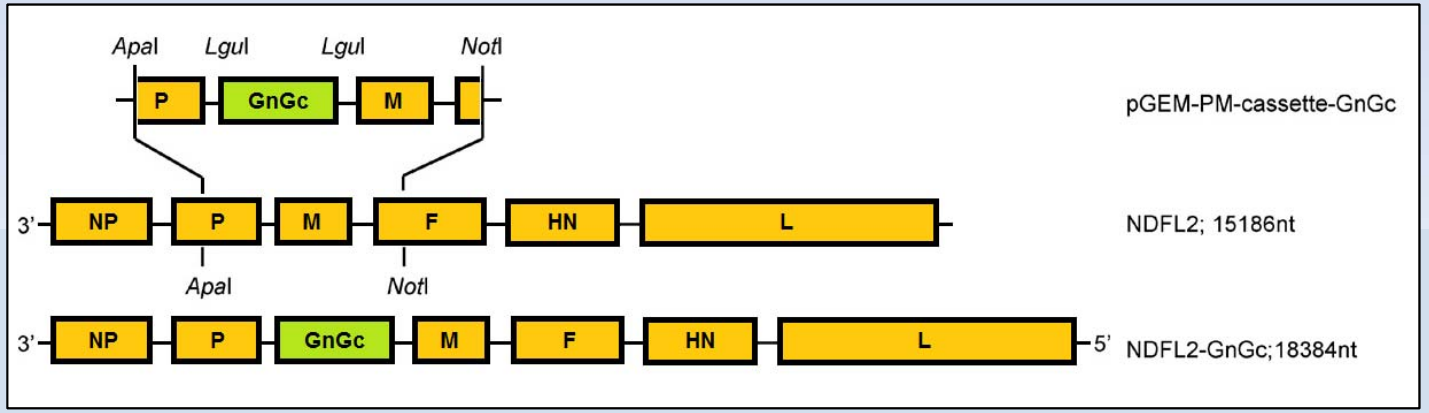
Progress towards registration:



NDV-vectored RVF vaccine

- Recombinant NDV (La Sota strain) containing Gn and Gc RVFV genes
- Developed by CVI
- Evaluated by Deltamune

Kortekaas et al. 2010a, 2010b



NDV-GnGc: Safety features

- **Excellent environmental safety profile**
- **ICPI = 0** (ICPI for lentogenic La Sota = 0.4)
- **No viraemia** (remains localised)
- **No clinical side effects** (neither mammals nor birds)
- **No spreading** (neither mammals nor birds)
- NDV-vectors - good safety profile in primates
- Negligible potential to gain virulence in field

NDV-GnGc: Vaccine efficacy

- Optimal dose: ~10^7 EID_{50} (single shot?)
- Modest levels Ab^{neut} [mice, sheep, cattle]
- Protect sheep against:
  - Viraemia: 100% (n = 8)
  - Clinical signs: 100% (n = 8)
- Duration of immunity: Durable - at least 5 months

- Future studies: Pregnant ewe challenge trials


Thank you for your attention!