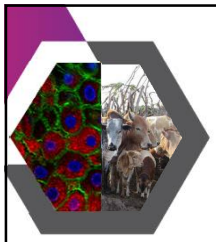

A new model for independent FMDV vaccine QA/QC as an aid to vaccine selection

Anna Ludi, Ginette Wilsden, Madeeha Afzal, Amin Asfor, Alison Burman, David Paton and Don King

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Biotechnology and Biological Sciences Research Council
Pirbright receives strategic funding from BBSRC UKRI

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Relationship Coefficient – r_1-values

- A measure of antigenic relatedness between a vaccine virus and a field strain
- r_1-value $\geq$ 0.3 indicates that there is a close antigenic relationship between the field isolate and vaccine strain. A potent vaccine containing this vaccine strain is likely to confer protection

$$\frac{\textit{Antibody titre of vaccine serum against field isolate (heterologous)}}{\textit{Antibody titre of vaccine serum against vaccine strain (homologous)}}$$

* Reports available at wrlfmd.org

2

Are r_1-values useful?

Efficacy of a high potency O_1 Manisa foot-and-mouth disease vaccine in cattle against heterologous challenge with a field virus from the O/ME-SA/Ind-2001 lineage collected in North Africa

Emma Fishbourne[a], Anna B. Ludi[a,*], Ginette Wilsden[a], Pip Hamblin[a], Bob Statham[a], Abdelghani Bin-Tarif[a], Emiliana Brocchi[b], Santina Grazioli[b], Aldo Dekker[c], Phaedra Eblé[c], Donald P. King[a]

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[c] Wageningen Bioveterinary Research, Laboratory Vesicular Diseases, Department of Virology, Houtribweg 39, 8221RA Lelystad, The Netherlands

Heterologous potency: 3.5 PD_{50} / dose

	homologous titre	heterologous titre	r_1- value
ALG/3/2014	2.80	1.90	0.13
BAR/14/2015	2.88	2.01	0.13
BAR/8/2015	2.88	2.22	0.22
BHU/1/2013	2.81	2.04	0.17
BHU/12/2012	2.34	1.42	0.12
LAO/3/2015	2.92	2.18	0.18
LIB/1/2013	2.93	2.04	0.13
LIB/17/2013	2.63	1.77	0.12
LIB/22/2013	2.63	2.[illegible]	0.38
LIB/7/2013	2.93	[illegible]	0.16
MOR/1/2015	2.41	[illegible]	0.27
MOR/2/2015	2.41	[illegible]	0.32
NEP/1/2014	2.70	[illegible]	0.16
NEP/13/2012	2.64	[illegible]	0.27
NEP/18/2013	2.70	[illegible]	0.20
NEP/18/2015	2.51	1.94	0.27
NEP/21/2012	2.70	1.77	0.12
NEP/6/2012	2.[illegible]	1.82	0.13
NEP/6/2013	[illegible]	1.92	0.16
NEP/6/2014	[illegible]	2.07	0.22
SAU/1/2013	[illegible]	1.94	0.14
SAU/1/2014	[illegible]	1.94	0.19
SAU/1/2016	[illegible]	2.04	0.39
SAU/4/2013	[illegible]8	1.96	0.15
SAU/6/2013	[illegible]70	2.13	0.27
SAU/7/2[illegible]	2.70	2.20	0.32
SAU/7/[illegible]	2.45	2.00	0.35
SRL/1[illegible]	2.76	2.12	0.23
SRL/1/2014	2.76	2.22	0.29
SRL/28/2014	2.70	2.10	0.25
SRL/30/2014	2.70	2.06	0.23
TUN/1/2014	2.66	1.89	0.17
UAE/1/2014	2.63	2.10	0.30
UAE/1/2015	2.38	2.01	0.43
UAE/2/2014	2.66	2.09	0.27
UAE/2/2016	2.52	2.05	0.34

r_1-value range 0.12 to 0.43

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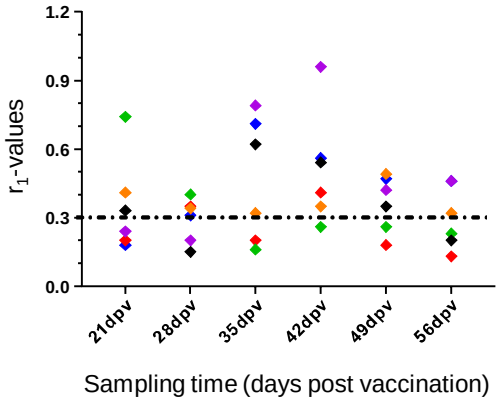
3

Limitation - Variation



*Slide courtesy of Jamaliah Bin Senawi

4

Additional Limitations…

Vaccine used to generate Bovine Vaccinal Sera (BVS)

High potency vaccine
Monovalent vaccine
21 days post vaccination
Single vaccine
Cattle

5

Additional Limitations

Vaccine used to generate Bovine Vaccinal Sera (BVS)

High potency vaccine
Monovalent vaccine
21 days post vaccination
Single vaccine
Cattle

However, vaccine used in the field is different and depended on the country's vaccine regime

small ruminants
booster vaccination?
low to high potency
sourced from different manufactures
polyvalent
pig
multiple vaccinations
cattle

6

A New Model

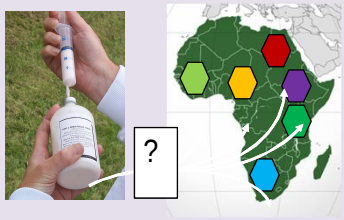
2019-2022

Activities linked to OIE twinning Project

7

The Challenge

- FMD viruses in Africa are antigenically diverse and vaccines used are of variable quality
- Lack of data to support vaccine selection and reports of failure in the field lead to poor trust in vaccines
- AU-PANVAC is mandated to provide independent quality control of all veterinary vaccines for Africa.



The project will establish and embed new tools to define whether vaccines are suitable for use in the different endemic pools in Africa

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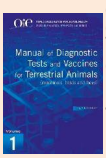
Licensed vaccine (Registration) → Production batches (Batch control) → Final product (Customer requirements)



Vaccine QA/QC Homologous

- Biosecurity and containment procedures
- GMP and in process controls
- MSV records
- Homologous potency testing in cattle
- Sterility, adventitious agent and innocuity testing
- Purity and safety testing
- Stability and duration of immunity
- Confirmation of MSV identity
- Sterility and innocuity tests
- Safety test
- Indirect potency test
- Monitoring of long-term storage conditions
- Verification of Ag integrity of batch
- Confirmation of batch identity
- Purity testing

VACCINATION PLAN

- Tender requirements
  - Shelf life
  - Antigenic relevance
  - Potency
  - Purity
  - Duration of immunity
  - Correlate of immunity threshold
- Verification /calibration studies

Vaccine performance Heterologous (field exposure)

- Selection of reference viruses (to cover regional risks)
- Generation of reference BVS
- Application of *in vitro* vaccine matching tests
- Development of harmonised test formats
- *In vivo* studies (where required)
- Identification of vaccine gaps
- Defining/validating heterologous correlates (cattle and other species)
- Batch testing to generate sera
- Confirmation that batch sera passes threshold heterologous responses
- Field studies of post-vaccination responses
- Vaccination coverage and outcomes
- Investigation of vaccine failure

KEY

- Vx Producers (with audit at registration/purchase)
- AU-PANVAC (with assistance from WRLFMD)
- Vx producer (with supervision/audit by AU-PANVAC) – or AU-PANVAC
- Customer (with support from FMD Reference labs/AU-PANVAC – where needed)
- OIE/FAO FMD Lab Network

BVI Botswana Vaccine Institute Ltd.

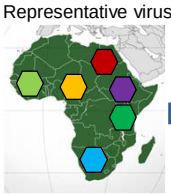
Boehringer Ingelheim

9

Project Vision

Developing a testing framework (with common metrics) that can accommodate vaccines from different suppliers

Representative virus panel



Surveillance → Reference Laboratories → Well characterized (sequenced) reference viruses

Generation of reference sera

Vaccine producer +/- PANVAC

AU-PANVAC suitability check

- Cross-neutralisation (VNT)
- New ELISAs (incl. affinity and IgG isotyping)

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Representative Viral Panel

with consultation of the OIE/FAO FMD Lab Network

OIE/FAO Foot-and-Mouth Disease Reference Laboratories Network

Vaccine performance will be assessed based on measurement of **heterologous titres** against viral lineages that pose threats to the region through the use of representative FMDV reference viruses

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Representative Viral Panel Approach

Sequencing of VP1 → Phylogeny

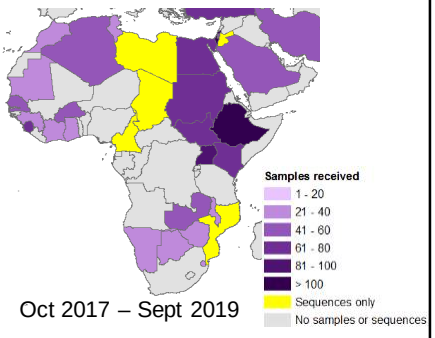
↓

VNT for using sera raised against diverse antigens

↓

Narrow down panel to focus unique antigenic phenotypes (at least 4 isolates/serotype)

African samples received by WRLFMD



Oct 2017 – Sept 2019

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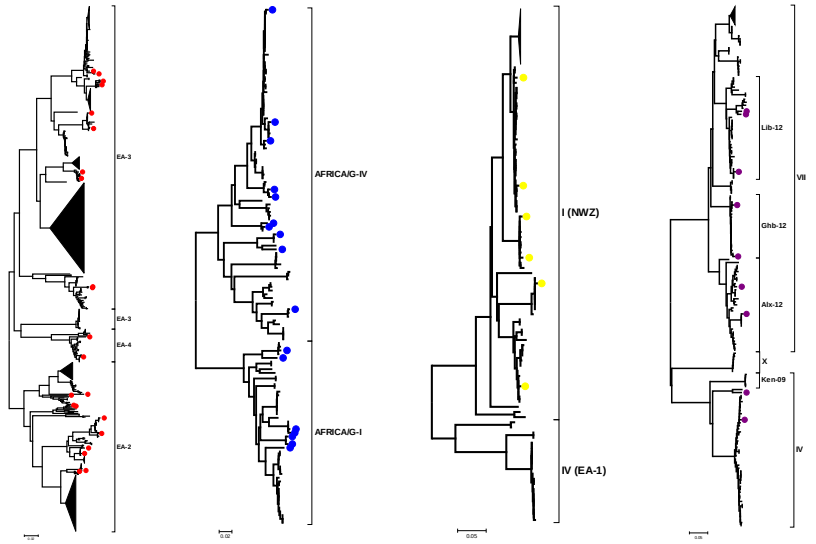
Representative Viral Panel Approach



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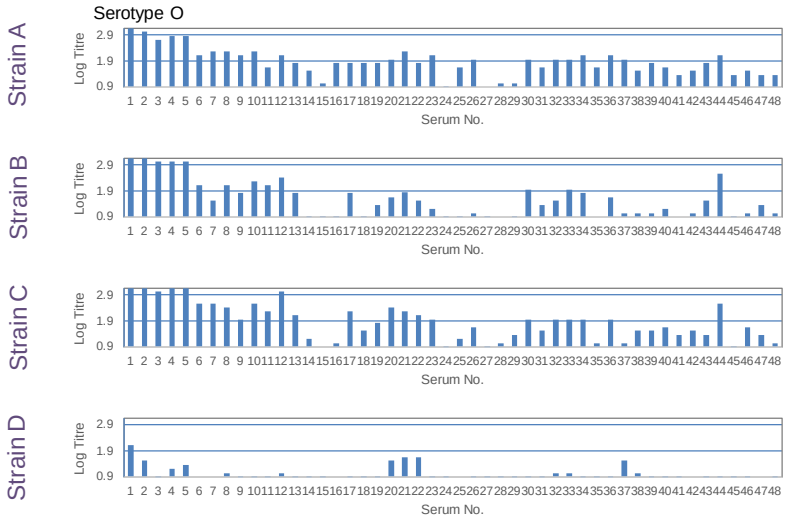
Representative Viral Panel Approach



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Reference Serum

- Well characterised bulk serum that can be used as a standard reagent between laboratories and industry
- Helps to identify the antigenic relationship when choosing the reference panel
- Helps calibrate and harmonise assays between laboratories

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Post Vaccination Serum

- Should use formulated vaccine that is used in the field
- The vaccinal serum could be produced in as few as five FMDV naïve cattle
- The vaccination regime should be identical to what is currently being done in the field and including day 0 and sera from any booster vaccination

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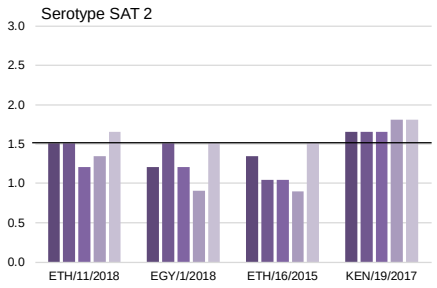
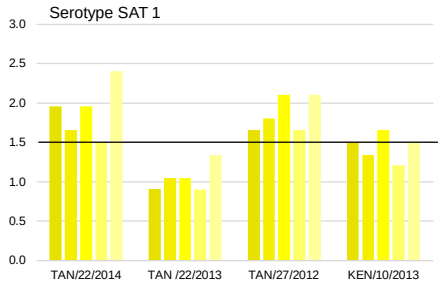
Post Vaccination Serum





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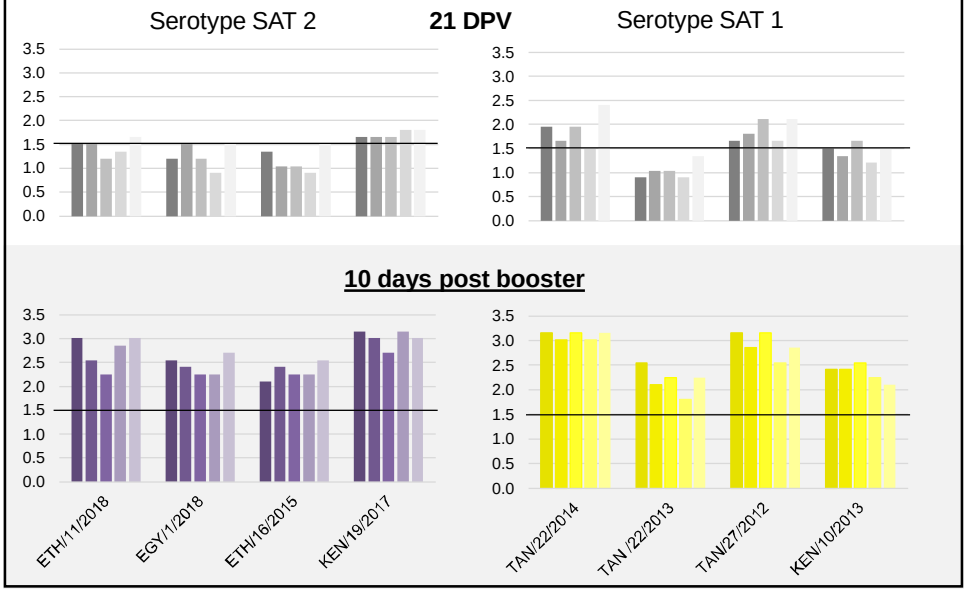
Post Vaccination Serum



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