Selecting the right tools

Vaccines, diagnostics, sanitary measures - why quality matters and how to select

Donald King

donald.king@pirbright.ac.uk

FAO World Reference Laboratory for FMD

WOAH Reference Laboratory for FMD

Acknowledgements: Valerie Mioulet, Nick Knowles, Anna Ludi, Britta Wood, Ginette Wilsden, Krupali Parekh, Andrew Shaw, Antonello Di Nardo, Jemma Wadsworth, Clare Browning, Mark Henstock, Hayley Hicks, David Paton, Nuredlina Prior, Dexter Wiseman, Ali Al-Rashed, Jozhel Baguisi, Harry Bull, Ryle Water, Deyzi Santos, Amy Sowood, Sarah Belgrave, Jessie Trussler

Work funded by:

Department for Environment Food & Rural Affairs

eufmd European Commission for the Control of Foot-and-Mouth disease

World Organisation for Animal Health Founded as OIE

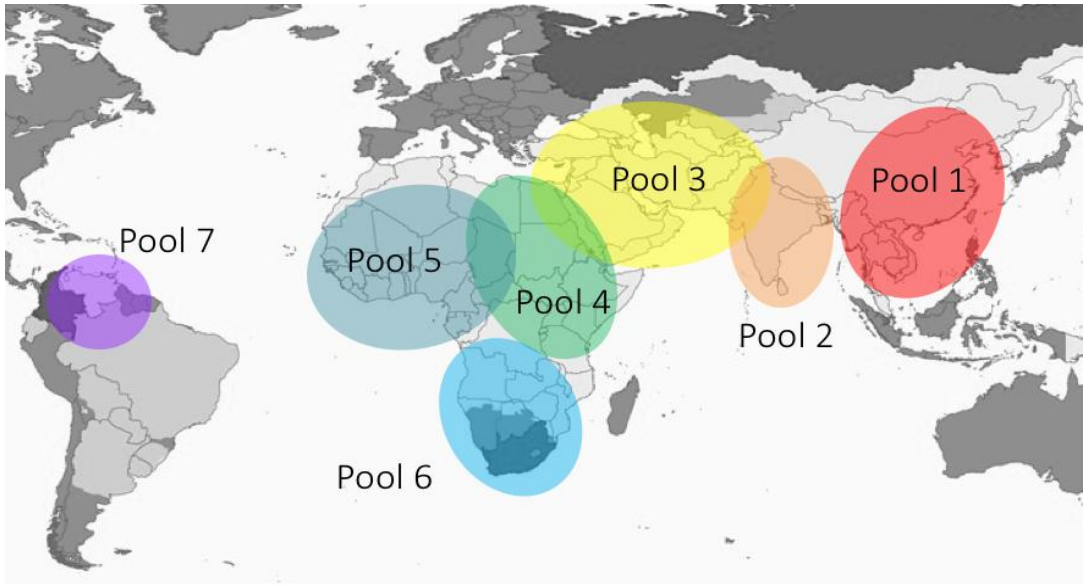
Gates Foundation

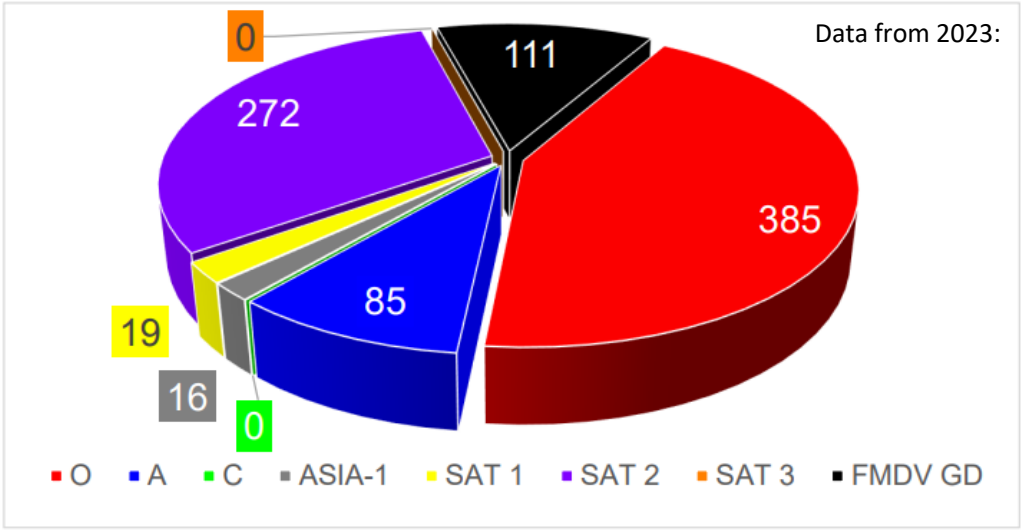
www.pirbright.ac.uk

FMD epidemiology: background

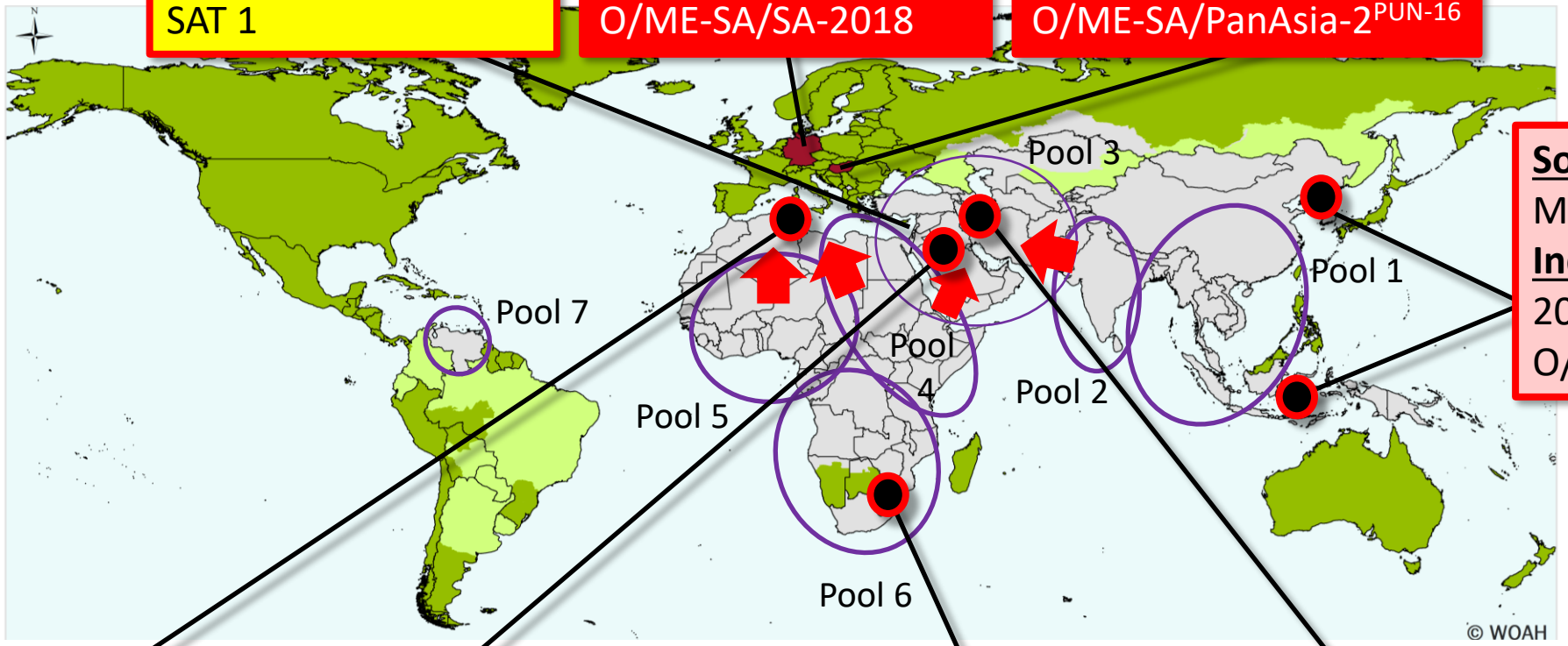
The epidemiology of FMD is dynamic, defined by:

- Seven virus ecosystems (Pools) that maintain specific FMDV strains requiring tailored diagnostics and vaccines
- Six circulating FMDV serotypes with an unequal distribution
  - Serotype C has not been detected globally since 2004
  - Serotype O is globally the most dominant serotype
- FMD control has led to FMD freedom in South America (except Venezuela)
- 2025: FMD incursions into Europe (O and SAT 1)
- Loss of FMD free status in Indonesia (2022) and countries in southern Africa (2021 -)





Headline global status for FMD (January 2026)



Cyprus
Dec 2025
SAT 1

Germany
Jan 2025
O/ME-SA/SA-2018

Hungary, Slovakia
Mar 2025
O/ME-SA/PanAsia-2^{PUN-16}

South Korea
March 2025
Indonesia
2024-25
O/ME-SA/Ind-2001e

Maghreb (2025)
O/EA-3

Algeria (2023/4)
SAT2/V

Middle East (2025)
SAT1/I and SAT1/III

Middle East (2023)
SAT2/XIV

Southern Africa
Serotype SAT2
(and SAT1 & SAT3)

Eswatini
SAT2

Iran, Iraq, Syria, Türkiye, Palestine, Pakistan, Israel
2023-2025
O/ME-SA/SA-2018

Tailored diagnostic tools…….

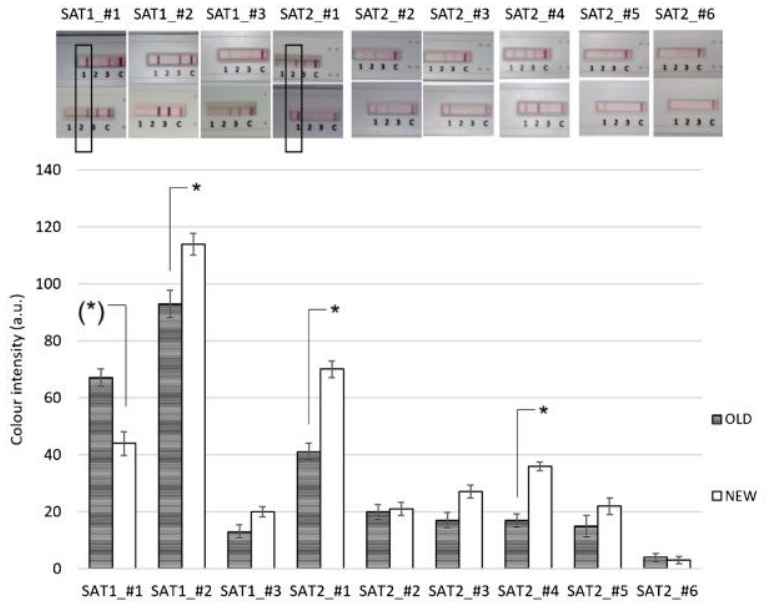
Antigen detection ELISA:

- Established test approach to define the serotype of a FMD virus in a sample
- Mab-based approaches are replacing Pab formats

LFDs:

- Pan-serotypic and serotype-specific versions of LFD are increasingly available (inc. from commercial sources)

- Lower analytical sensitivity compared to PCR –based tests
- Serotype-specificity is defined by the reactivity of the antibody reagents – scope for cross-reactivity should be considered
- Importance of test redundancy

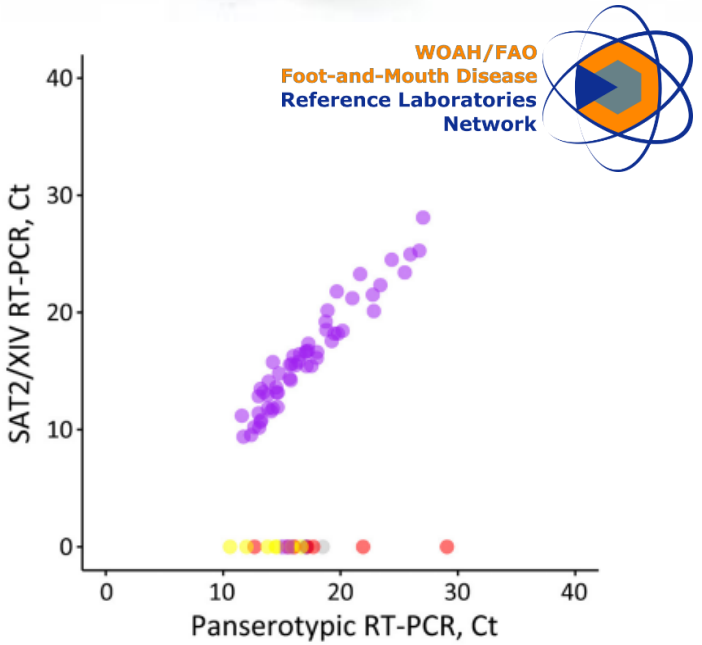


Cavalera et al., (2024) Micro Acta **191**:9

Tailored diagnostic tools…….

Lineage-specific real-time RT-PCRs

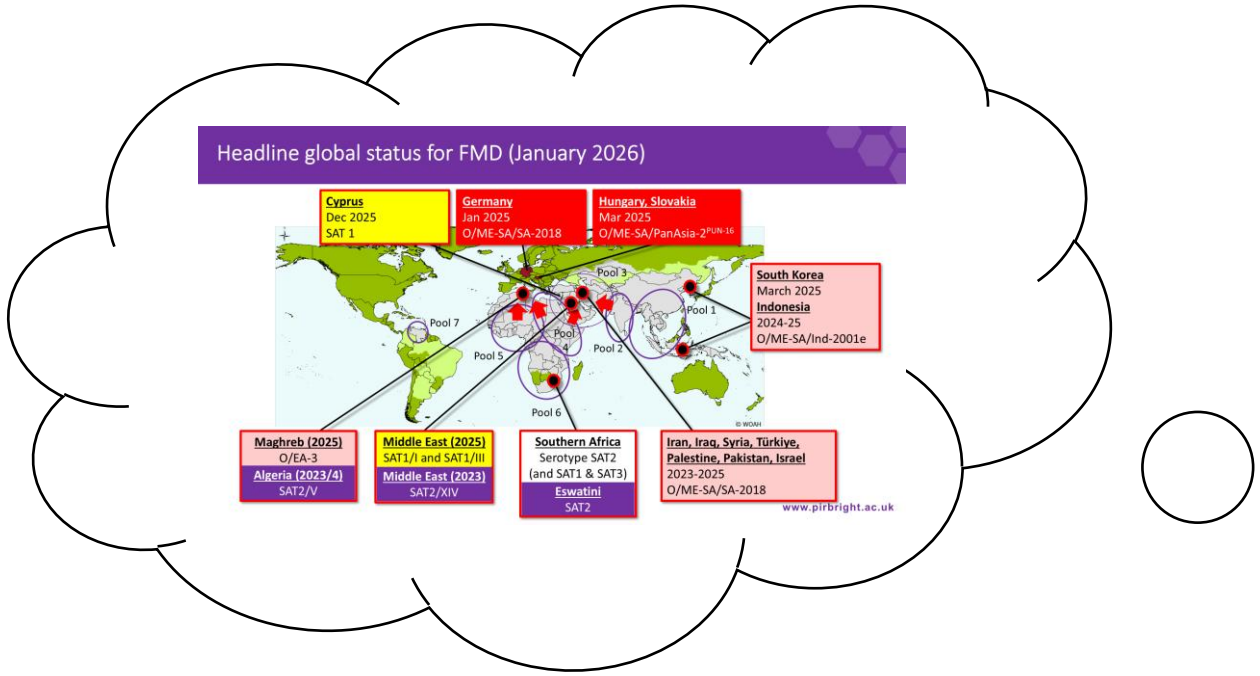
- *Toolbox* of assays from different laboratories
  - Ahmed (2012) TBED; Bachanek-Bankowska (2016) JVM; Chestley (2022) FVS; El Bagoury (2022) JVM; Jamal (2015) PLoS One; Lim (2022) TBED; Reid (2014) JVM; Saduakassova (2018) JVM
- Ability to *rapidly* identify the particular FMDV lineage that is present in a sample
- Designed to be run along-side the pan-serotypic real-time RT-PCR assays described in the WOAH Manual
- Could be used where sequencing capacity is not available
- Ensure primers/probe remain fit-for-purpose (https://www.foot-and-mouth.org/science/lineage-specific-fmdv-real-time-rt-pcr-assays)



Di Nardo et al., (2025) EID **31**: 370

FMD vaccines

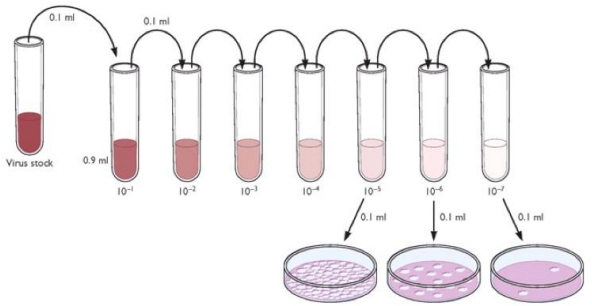
- Vaccines are produced by inactivation of FMDV isolates grown in cell culture
- > 2 billion doses administered annually
- Success in Europe and South America show that vaccination is an important tool to control and eradicate FMD
- **Need to cover multiple serotypes and antigenic variants**
- **FMD vaccines are not a standard product and can have variable quality** (i.e., different producers use different master seed strains, at different antigen payload, with different formulation regimes)
- **Protective 146S antigen (intact FMDV capsid) is unstable**

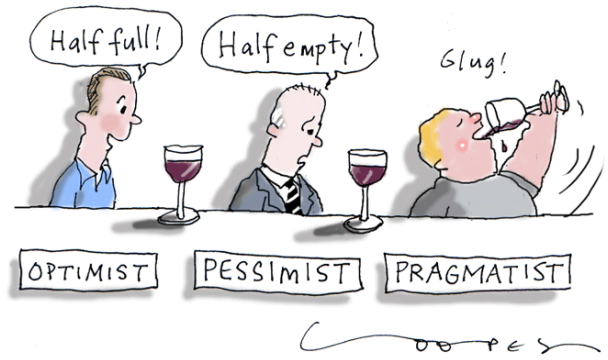


- Which FMD vaccine should I purchase?
- How can I ensure that it is fit for purpose? (i.e., will it be efficacious for the specific FMD viruses that threaten my livestock)

Approaches for FMD vaccine selection

- Effective vaccines need to provide relevant heterologous (cross) protection against field strains – cross neutralisation
- In-vitro vaccine matching (WOAH Manual - Chapter 3.1.8)
  - Compares the ability of defined bovine vaccinal sera (BVS) to neutralise field strains vs a **single** homologous vaccine strain
  - Can be performed by **VNT** or LPBE
  - R-value ≥ 0.3 indicates that there is a close relationship between the field isolate and vaccine strain – A potent vaccine containing this vaccine strain is likely to confer protection
  - **VM results are inherently variable (when the VNT is used)**
  - **Not a quantitative test**
  - **<u>Test multiple field viruses from related outbreaks</u>**





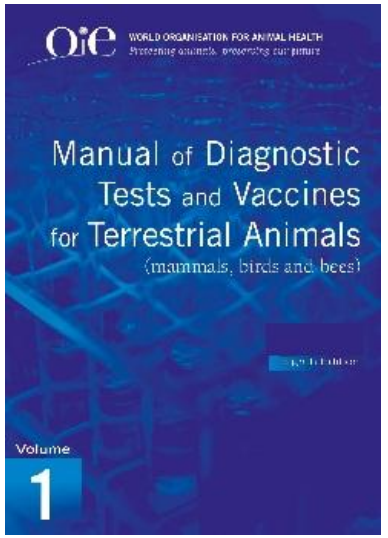
Vaccine selection for endemic settings

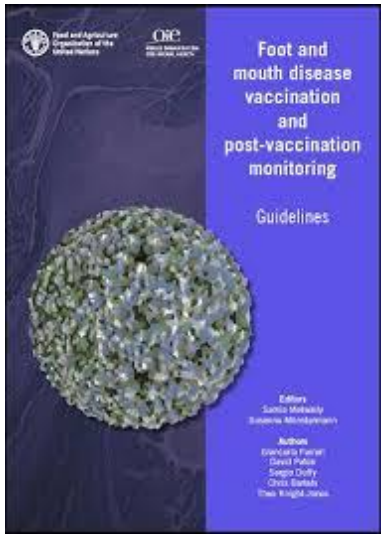
Obvious gaps and challenges:

1. Vaccine-matching (r_1-values) considers strain suitability but NOT the quantity/quality/combinations of antigens in a final product (and is limited due to access to vaccine strains and BVS)
2. WOAH Terrestrial Manual focus on homologous of monovalent vaccines vs heterologous vaccine performance that is required **in the field** with multivalent products

Increasing focus of testing:

- Measurement of **heterologous responses**
- Using **formulated product supplied to customers**
- Use common/standardized FMDV viruses (**Antigen Panels**) representative of the antigenic threats in a region – proposal for reference antigens for East Africa (https://www.wrlfmd.org/node/2096/)





East Africa antigen panel

- Paper published in May 2025
- Candidate viruses for the other FMD endemic pools have been selected

npj | vaccines

Article

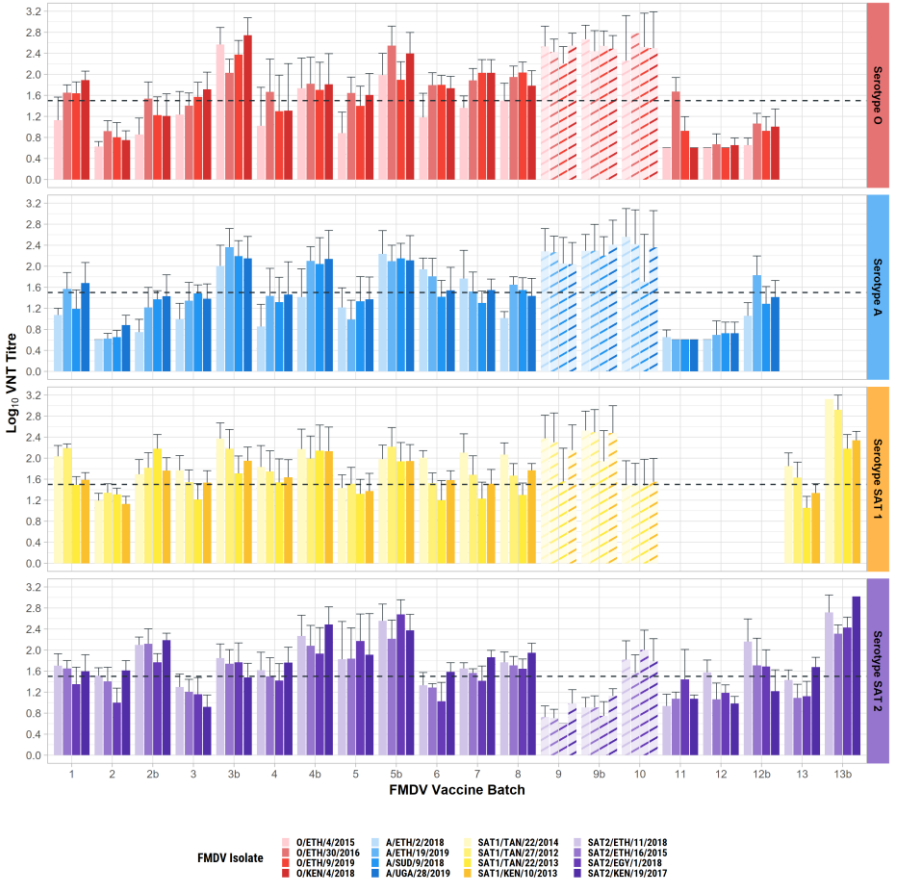
Published in partnership with the Sealy Institute for Vaccine Sciences

https://doi.org/10.1038/s41541-025-01128-7

An antigen panel to assess the regional relevance of foot and mouth disease vaccines

Check for updates

David J. Paton[1] ✉, Ginette Wilsden[1], Clare FJ Browning[1], Efrem A. Foglia[2], Antonello Di Nardo[1], Nick J. Knowles[1], Jemma Wadsworth[1], Simon Gubbins[1], Ethel Chitsungo[3], Cisse Rahamatou Moustapha Boukary[3], Gelagay Ayelet[3], Charles S. Bodjo[3], Nick Nwankpa[3], Emiliana Brocchi[2], Santina Grazioli[2], Anna Ludi[1] & Donald P. King[1]



World Organisation for Animal Health
Founded as OIE

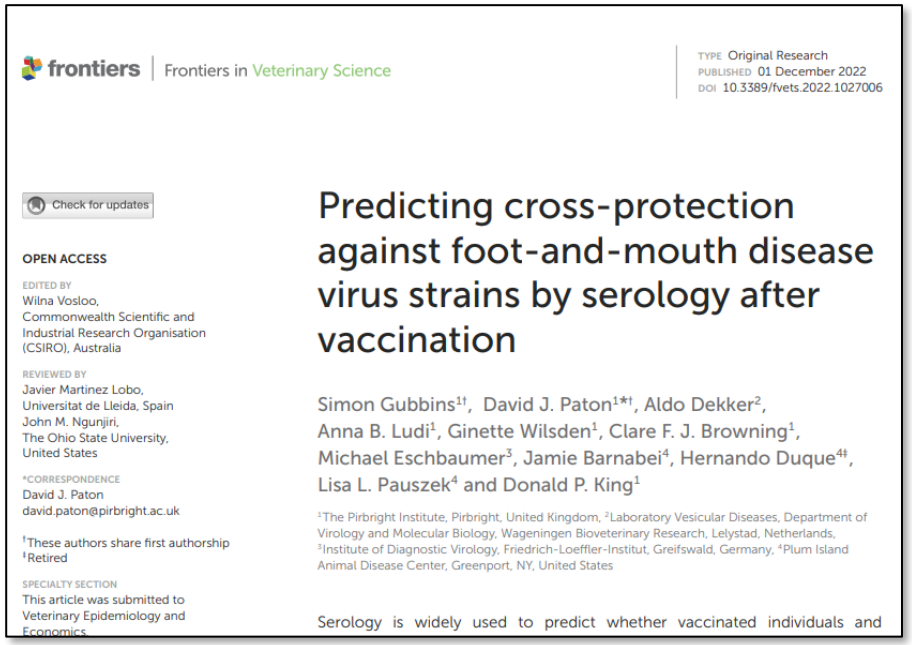
AU-PANVAC
Pan African Veterinary Vaccine Center of African Union

- Experience tells us that neutralising antibodies are correlated to protection, but
- …..how much FMD-specific antibody is enough?

Estimating heterologous serological cut-offs

Be pragmatic:

Precise determination is not needed to identify poor quality vaccines!



frontiers | Frontiers in Veterinary Science

TYPE Original Research
PUBLISHED 01 December 2022
DOI 10.3389/fvets.2022.1027006

Check for updates

OPEN ACCESS

EDITED BY
Wilna Vosloo,
Commonwealth Scientific and Industrial Research Organisation (CSIRO), Australia

REVIEWED BY
Javier Martinez Lobo,
Universitat de Lleida, Spain
John M. Ngunjiri,
The Ohio State University, United States

*CORRESPONDENCE
David J. Paton
david.paton@pirbright.ac.uk

†These authors share first authorship
‡Retired

SPECIALTY SECTION
This article was submitted to Veterinary Epidemiology and Economics

Predicting cross-protection against foot-and-mouth disease virus strains by serology after vaccination

Simon Gubbins[1†], David J. Paton[1*†], Aldo Dekker[2], Anna B. Ludi[1], Ginette Wilsden[1], Clare F. J. Browning[1], Michael Eschbaumer[3], Jamie Barnabei[4], Hernando Duque[4‡], Lisa L. Pauszek[4] and Donald P. King[1]

[1]The Pirbright Institute, Pirbright, United Kingdom, [2]Laboratory Vesicular Diseases, Department of Virology and Molecular Biology, Wageningen Bioveterinary Research, Lelystad, Netherlands, [3]Institute of Diagnostic Virology, Friedrich-Loeffler-Institut, Greifswald, Germany, [4]Plum Island Animal Disease Center, Greenport, NY, United States

Serology is widely used to predict whether vaccinated individuals and

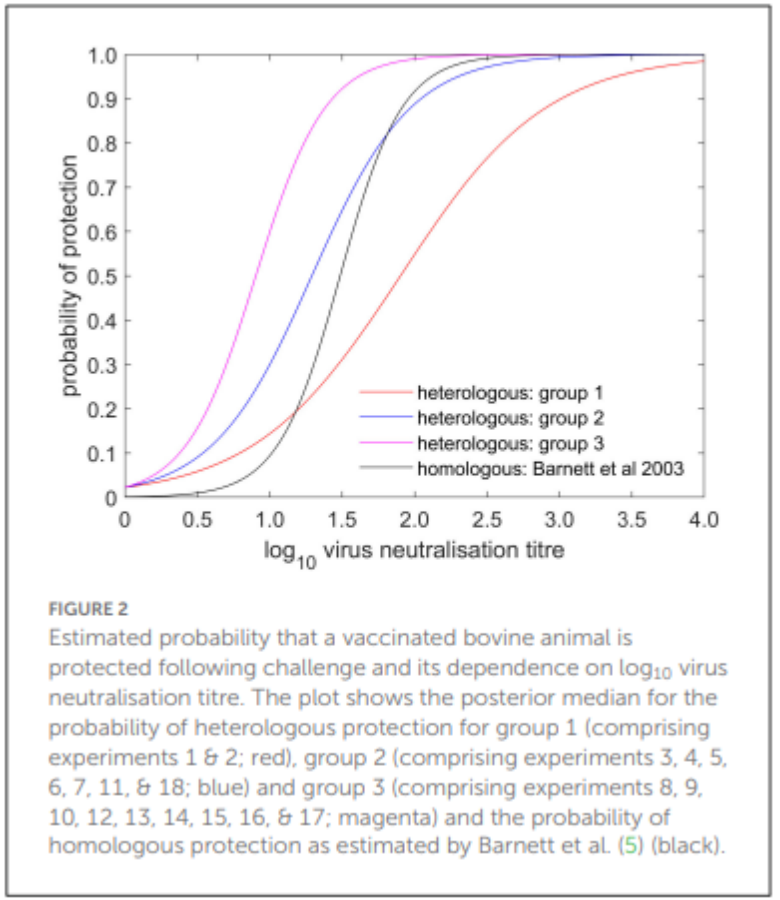
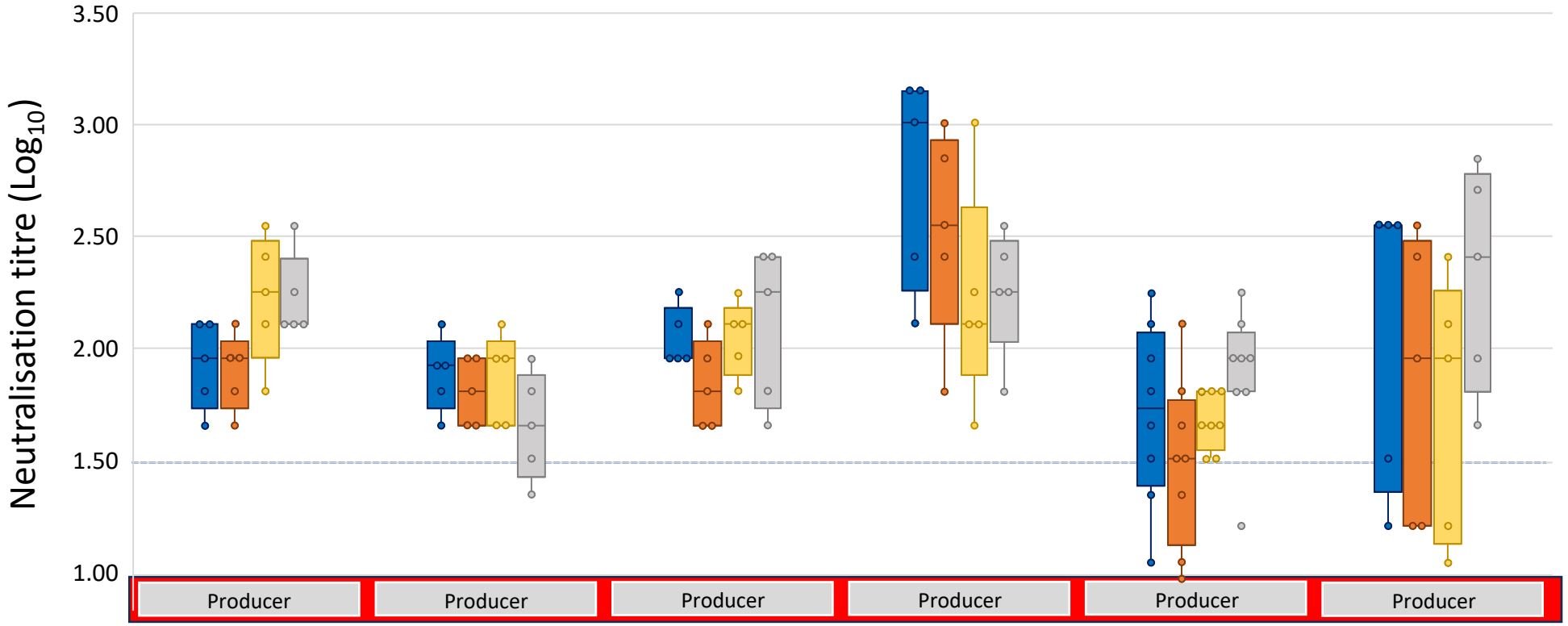


FIGURE 2
Estimated probability that a vaccinated bovine animal is protected following challenge and its dependence on $\log_{10}$ virus neutralisation titre. The plot shows the posterior median for the probability of heterologous protection for group 1 (comprising experiments 1 & 2; red), group 2 (comprising experiments 3, 4, 5, 6, 7, 11, & 18; blue) and group 3 (comprising experiments 8, 9, 10, 12, 13, 14, 15, 16, & 17; magenta) and the probability of homologous protection as estimated by Barnett et al. (5) (black).

- Day-of-challenge sera (n = 180) from 13 previous FMD cross-protection experiments for serotypes O (n = 2), A (n = 10), and SAT 2 (n = 1)
- Sera retested at WRLFMD

Selecting vaccines for the Middle East (Pool 3)

Heterologous responses of SAT1 vaccines against SAT1/I field isolates



Biogénesis Bagó	DOLLVET	Boehringer Ingelheim	Biopharma	KEVEVAPI	BVI
SAT1 2020	SAT1/BOT/1/77	SAT1/RHO-78	O/A/SAT1/SAT2	SAT1 T155	SAT 109
30dpv	21dpv	21dpv	21dpv	21dpv	35dpv
n=5	n=5	n=5	n=5	n=8	n=5

eufmd
European Commission for the Control of Foot-and-Mouth disease

Viral antigens
- BAR/50/2025
- IRQ/11/2025
- QTR/7/2023
- TAN/22/2014 *

*East Africa reference antigen (Paton et al., 2025)

Source of sera

Sera collected Day post-vaccination

NB: Some of the sera used for this testing was generated from trial-blends of vaccines and therefore customers are advised to carry out in-country testing with the final formulated product to confirm that responses in vaccinated animals achieve these levels of FMDV-specific antibody.

Why FMD vaccines fail?

- **Poor quality vaccine (potency, 146S content)**
- **Poor antigenic match to the circulating strains**

- Failure in the cold chain
- Low coverage in the target population
- Failure to follow recommended vaccination schedules (two doses in the primary course)

FMD has potential for very high transmissibility (estimated R_o 2-70)

- Failure to employ complementary control measures – movement controls

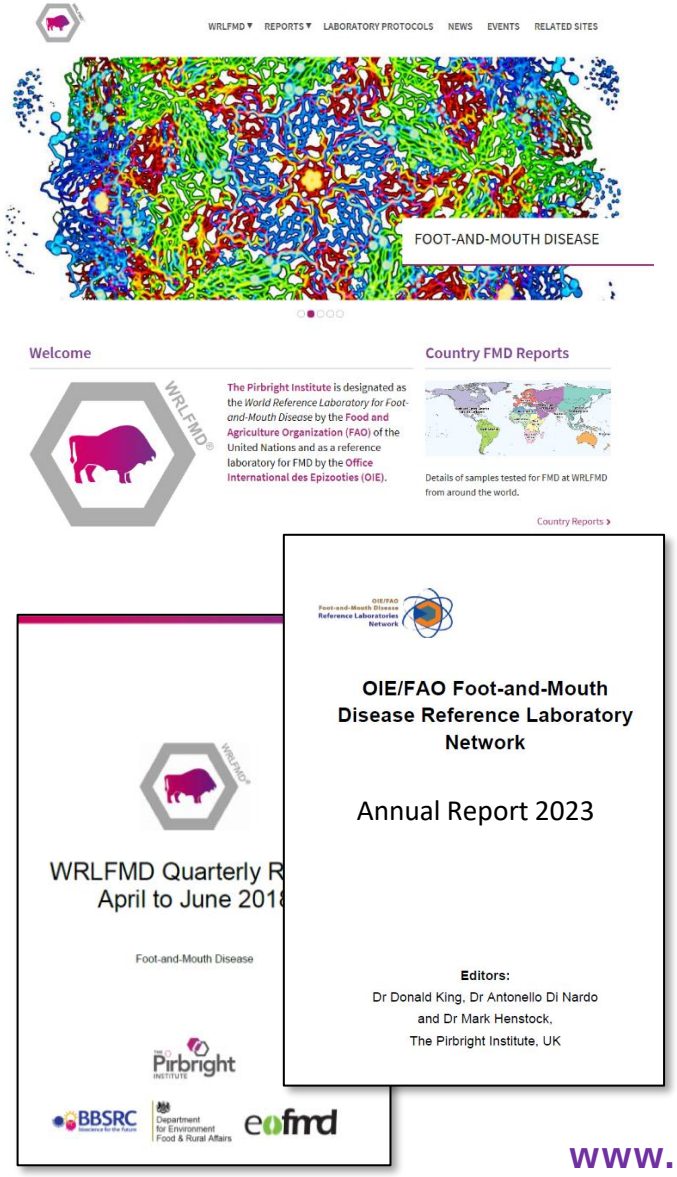
Some real-world experiences

Summary and concluding remarks

- FMD diagnostic approaches need to consider the range of FMDV serotypes (and look-a-like diseases)
  - **Local validation** of these tests is important to ensure that they are fit for purpose
- FMD vaccines are unique
  - Need to cover different serotypes and antigenic variants
  - Producers supply vaccines that utilise different vaccine master-seed strains
  - Often formulated to contain multiple antigens (serotypes/strains)
  - FMD vaccines are difficult to produce and the antigen is unstable
  - New immunoassays that directly measure 146S content are being developed/validated
- Use of **poor-quality** vaccine leads to **poor trust** in FMD vaccination campaigns
- **Testing** of FMD vaccines is very important - providing evidence to stakeholders (investors, farmers) to demonstrate:
  - Selected vaccine provides cross-protective responses to FMD viruses circulating in the field
  - Batch-to-batch consistency of the vaccine
  - Post-vaccination monitoring to verify maintenance of the cold chain of the formulated vaccine, and to ensure adequate herd-level coverage and duration of immunity in the target species

Further information……

- FMD reports and lab testing (https://www.wrlfmd.org/ref-lab-reports)
    - *Genotyping reports*, *Vaccine matching* and *Serotyping reports*
- Other data sources:
    - Quarterly WRLFMD/EuFMD report (https://www.wrlfmd.org/ref-lab-reports)
    - Annual report of the WOAH/FAO FMD Laboratory Network (http://foot-and-mouth.org/)
    - OpenFMD (www.openfmd.org) – sequences, genotyping, vaccine selection and surveillance



Thanks:

- TAFS for supporting my attendance at this meeting
- Collaborating FMD Reference Laboratories and field teams
- Partners within the WOAH/FAO FMD Lab Network
- Support for the WRLFMD and research projects

Indirect/immunogenicity studies to assess vaccine performance

FMD vaccine
Commercial batches within shelf-life - multi-valent
Supplied directly from company*
Cold chain monitored with temperature logger

Options:
1. Conducted in a FMD-free country ($$)
2. NSP antibody testing

Naïve animals
Not vaccinated
Not Infected
>6 months of age

Sera collection
21 (or 28) dpv

Booster dose
(according to the schedule recommended by the producer)

Sera stored at -20 °C

Sera collection
10 (or 28) dprv

Sera tested by VNT
Titres against FMD viruses that pose a risk to the target population
Regional reference antigens