FMD vaccines

Donald King
donald.king@pirbright.ac.uk

UK National Reference Laboratory for Vesicular Diseases
FAO World Reference Laboratory for FMD (WRLFMD)
WOAH Reference Laboratories for FMD and SVD

Department for Environment Food & Rural Affairs

World Organisation for Animal Health
Founded as OIE
FMD Reference Laboratory

Foot-and-Mouth Disease

- Affects cloven-hoofed livestock and related wildlife species
- FMD is difficult to control
  - Short incubation period
  - Rapid replication
  - High susceptibility of hosts
  - Direct and fomite transmission routes
- Seven serotypes (O, A, Asia 1, SAT1, SAT2, SAT3 and C)
- Annual Impact* of FMD
  - Production losses and vaccination:
    ($ 6.5-21 billion)
  - Incursions into FMD-free countries (>$1.5 billion)

*estimated by Knight-Jones and Rushton 2013

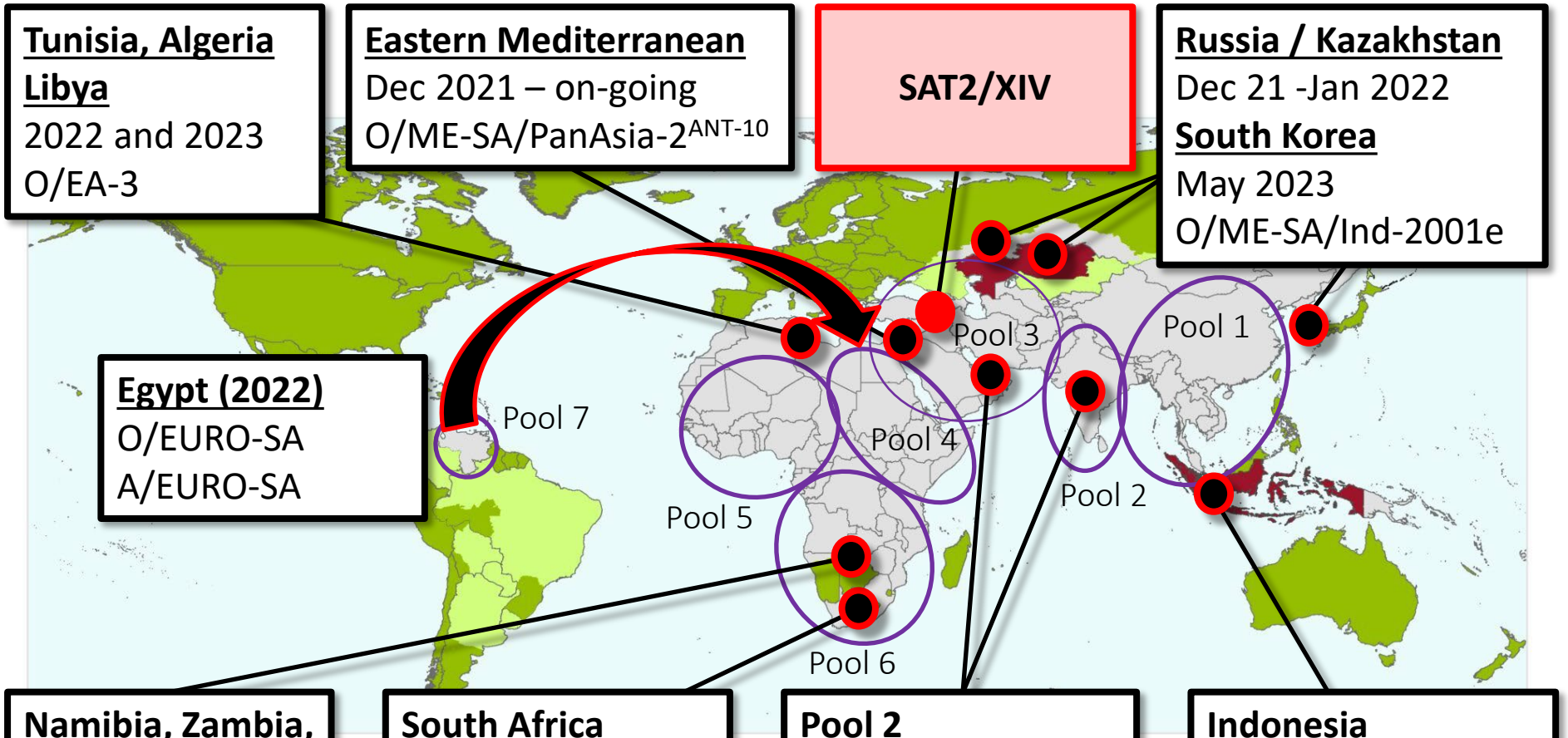
(Pictures by E. Ryan, J Gloster)

tongue lesion

interdigital foot lesion

Headline global events (2021/23)

https://www.wrlfmd.org/ref-lab-reports



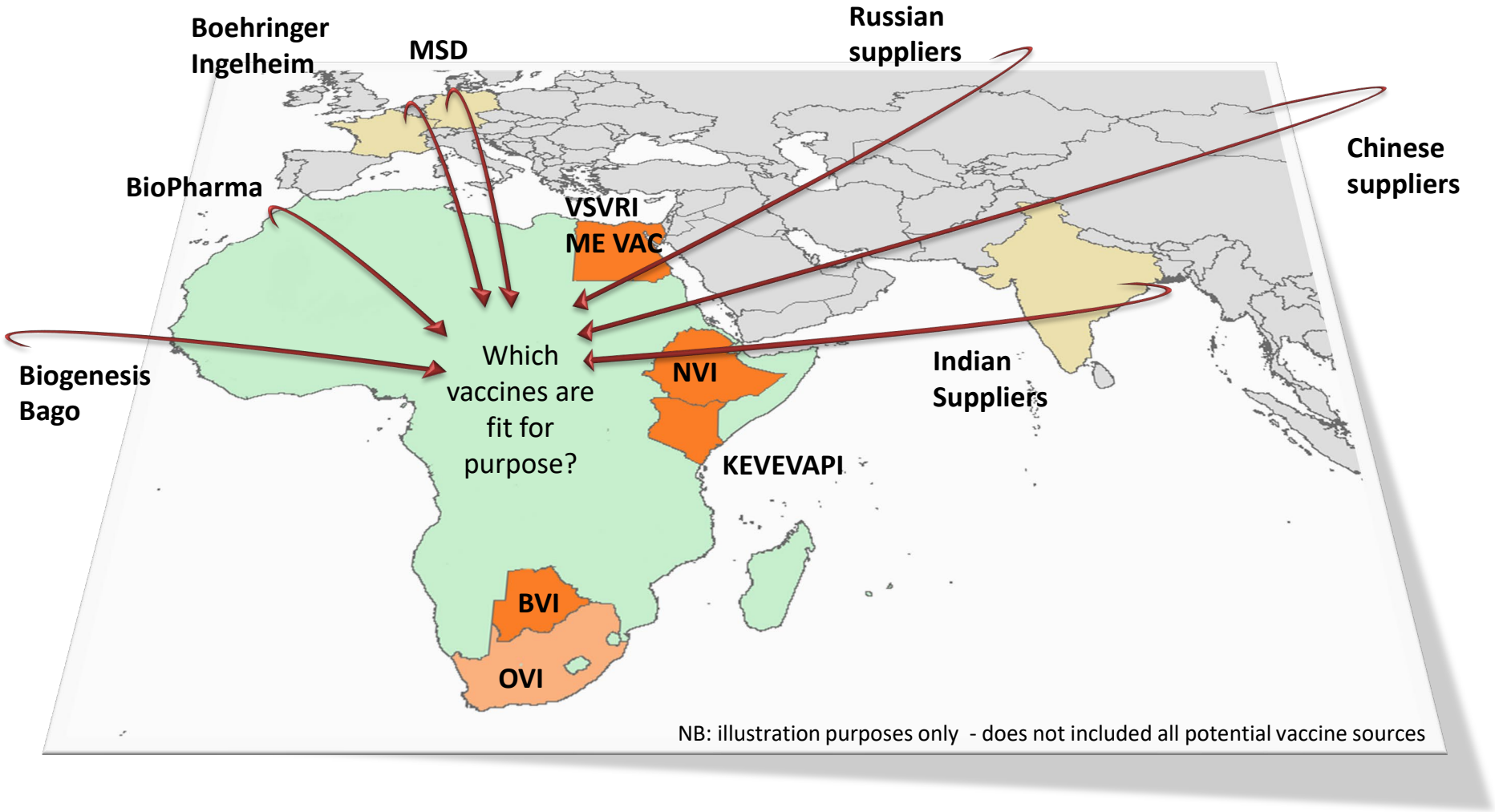
WOAH Map – March 2023

FMD vaccines

- Vaccines 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**
- **Protective 146S antigen (intact FMDV capsid) is unstable**

Selection of FMD vaccines is complex

(different antigens, formulation, potency)



Inherent genetic (and antigenic) diversity in field viruses from different FMD serotypes (O, A, SAT 1, SAT 2 [SAT 3])

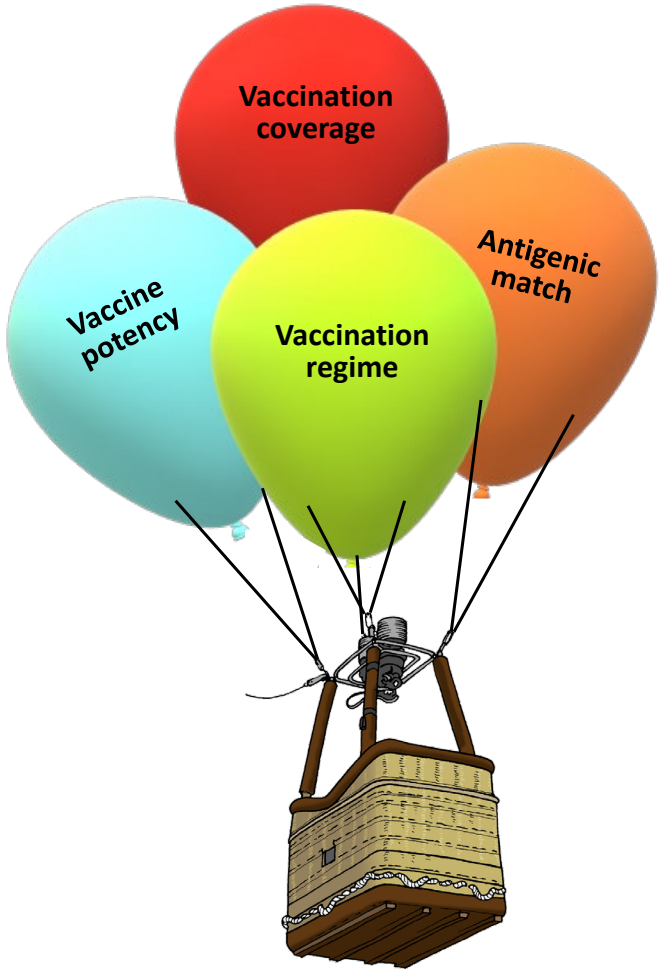
FMDV vaccine selection

Approaches

- In-vitro vaccine matching (www.wrlfmd.org)
  - Vaccine matching is performed by measuring whether antibodies generated by the vaccine will react to the field virus
  - Compares the ability of bovine vaccinal sera to neutralise field strains vs a **single** vaccine strain
  - r_1-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
  - **Not a quantitative test**
- In-vivo vaccine cross-protection studies (heterologous)
- Small-scale immunogenicity studies
- Field evaluation

Use of vaccine matching data

- Antigenic-match (vaccine-matching) is not the sole determinant of whether a vaccine will work!
  - Vaccine potency
  - Vaccination regime (one dose/two dose)
  - Vaccine coverage in the target population
- **Post vaccination monitoring is important!**



Vaccine failure

Vaccine selection: challenges

Obvious gaps:

1. The quality and performance of FMDV vaccines cannot be easily assessed through **direct** testing – immunisation of animals usually needed
   - New tools are being developed to directly assess 146S content of vaccines (nanobodies and Mab-based tests)
2. Vaccine matching is only performed on a limited number of vaccines
3. Homologous/monovalent QA/QC (WOAH Manual) vs heterologous vaccine performance **in the field** with multivalent products
   - Adoption of regional reference antigens (e.g. see: https://www.wrlfmd.org/node/2096/) can be used to assess/compare antibody responses for formulated FMD vaccines

New FMD vaccines

Gaps addressed by current near-market technologies:

- Increased biosafety (not derived from infectious FMDV)
- FMDV capsids with improved stability
- Improved DIVA capability
- **High-quality vaccines at a lower price**

Platform technologies:

- Stabilised empty VLPs
- L-deletion vaccine strains
- RNA vaccines
- Adenovirus vectored vaccines

Continued challenges:

- Longer duration of immunity
- Wider strain specificity