2012 GFRA Workshop Surveillance, Epidemiology, Vaccination and Control of FMD. Hazyview, S. Africa,17 to 19 April 2012

FMDV Antigenicity And Vaccine Matching Studies

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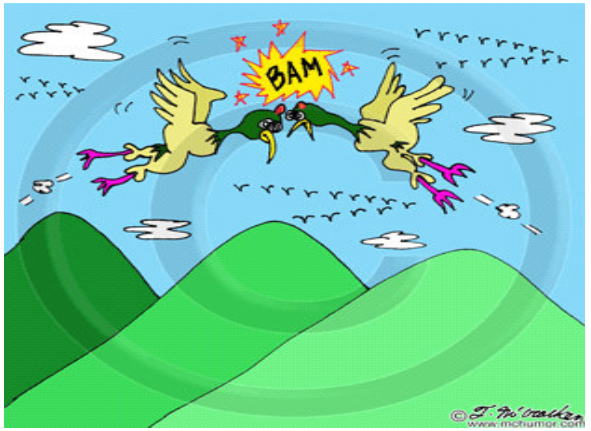
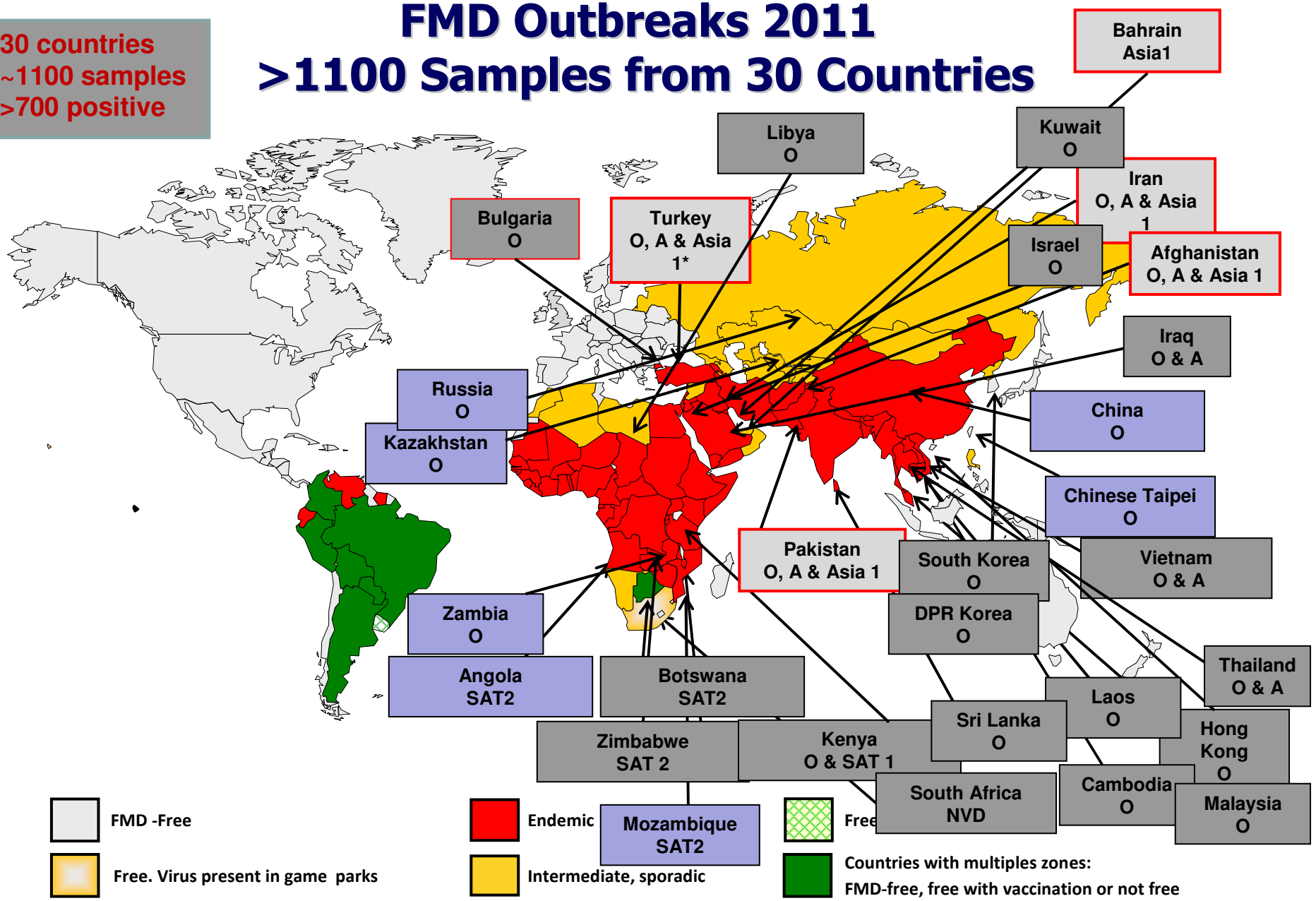
Outline

- FMD global situation
- Current approaches for vaccine matching studies
- Monitoring FMDV antigenicity deviation by serology
- r_1 values and vaccine potency tests



FMD Outbreaks 2011
>1100 Samples from 30 Countries

30 countries
~1100 samples
>700 positive

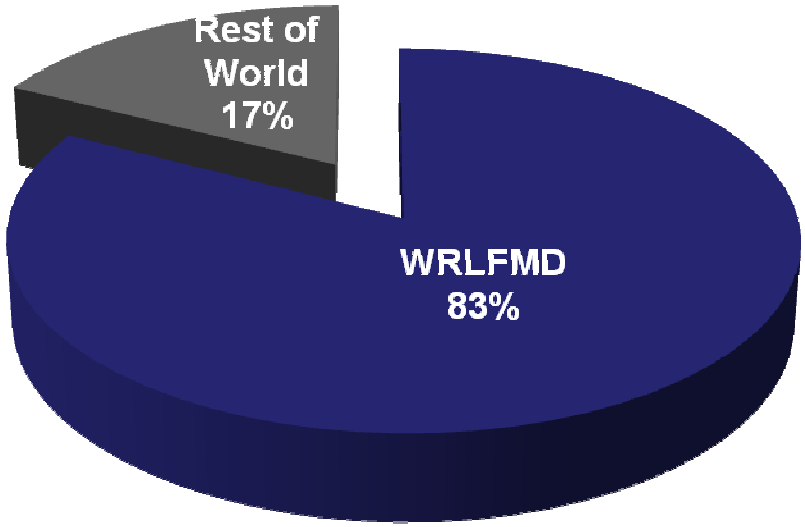


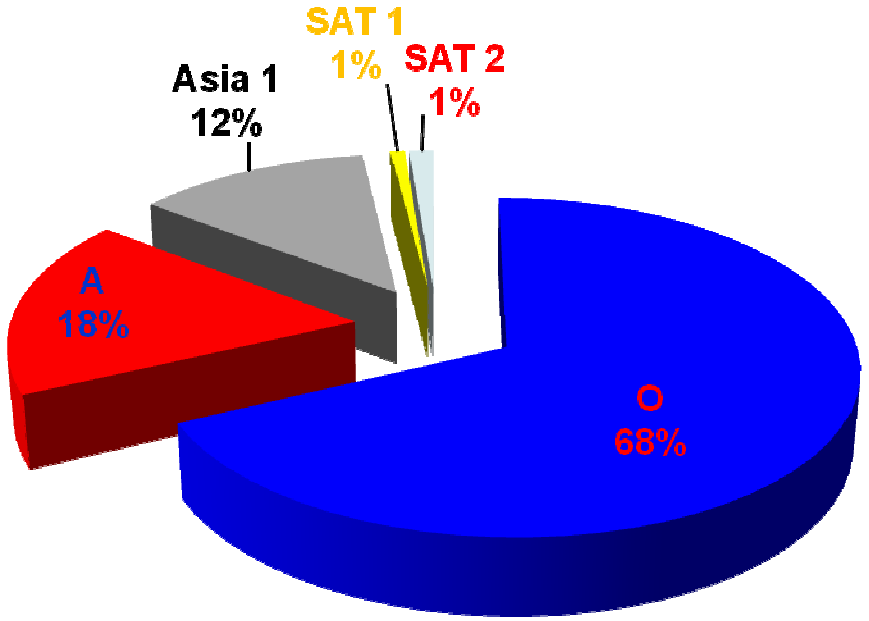
Samples Analysis in 2011

660VP1 sequences were reported in 2011:

545 (83%) came from WRLFMD

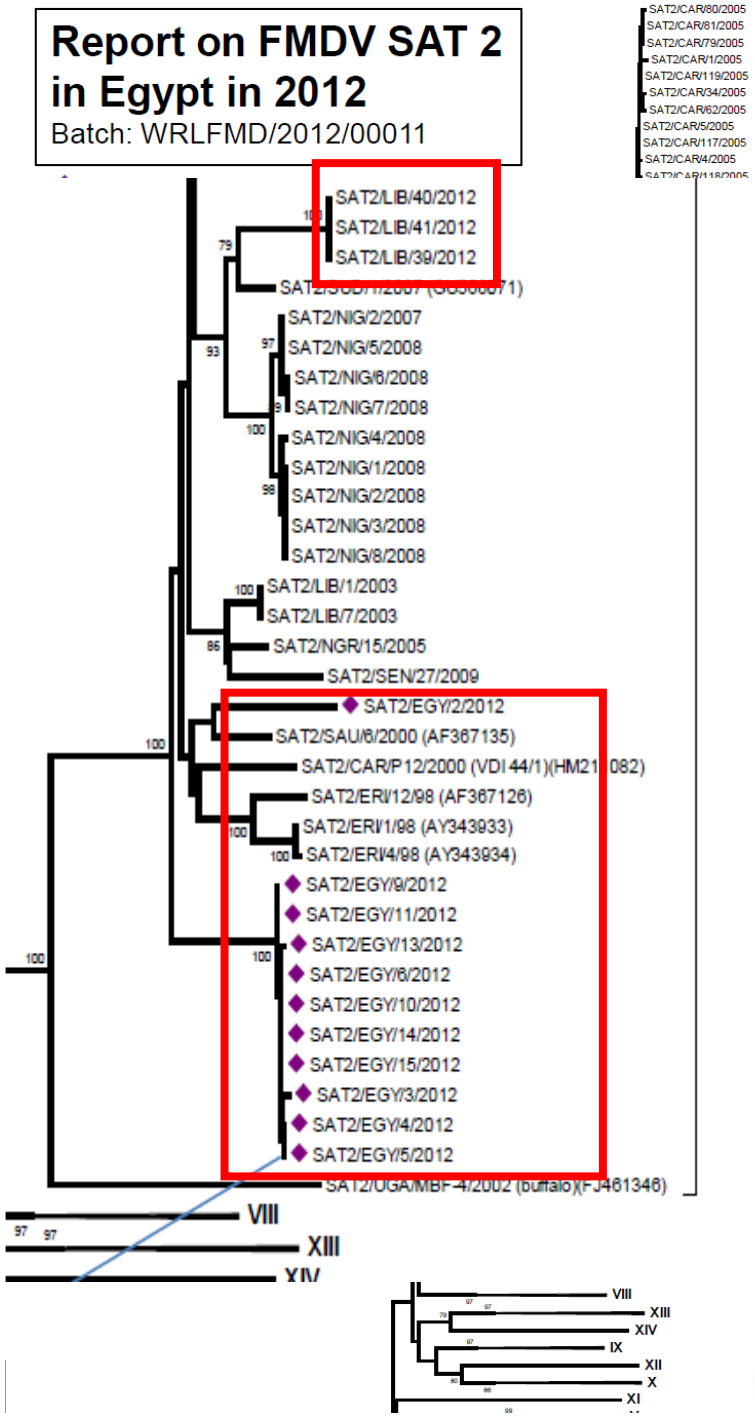
The remaining 115 (17%) came from other laboratories



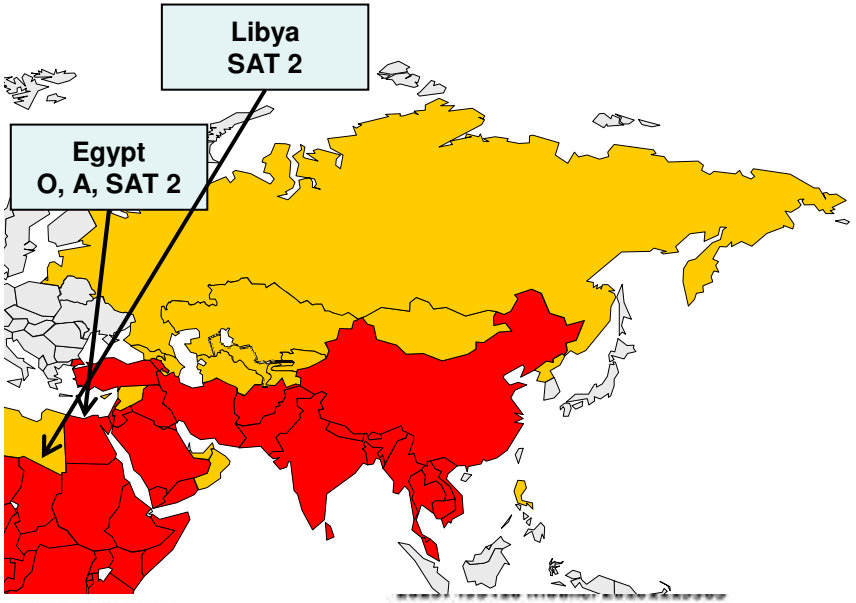


Report on FMDV SAT 2 in Egypt in 2012

Batch: WRLFMD/2012/00011



FMD Outbreaks 2012



Date Received: 12th March 2012
Country of Origin: Egypt
Date Reported: 26th March 2012

Report no:	2dmVNT		
Vaccine:	2dmVNT	Sat2 Eri	Sat2 Zim
Field Isolate:	test ref:		
Sat2 Egy 6/2012	mean	0.62	0.20
Sat2 Egy 9/2012	mean	0.46	0.15

Report no:	2dmVNT		
Vaccine:	2dmVNT	Sat2 Eri	Sat2 Zim
Field Isolate:	test ref:		
Sat2 Lib 40/2012	mean	0.25	0.19
Sat2 Lib 41/2012	mean	0.26	0.14

WRLFMD

Vaccine Selection for Control of FMD

- The potency of the vaccine
- Antigenicity of the vaccine to be used
  - The virus is antigenic diverse: not cross protective between subtypes within a serotype, and antigenic changes due to mutation and recombination
- Importance of vaccine matching
  - Disease outbreaks in properly vaccinated animals
    - A Iran 05 strain cases in A Iran 96 vaccinated cattle in Middle East
    - SAT 2 outbreaks in Botswana despite use of a trivalent vaccine
    - O PanAsia 2 in Turkey and Iran
  - A problem of efficacy of vaccination or vaccine matching?

Vaccine Matching (Strain Differentiation) of FMDV

- Characterize the antigenic relationship between field strains of a specific serotype to a vaccine strain known to convey protection against a broad spectrum of subtypes of that serotype

- To allow rational choice of vaccine strains to ensure the antigens/vaccines will be effective in the event of an outbreak of FMD

- To identify the antigenic deviation and to select a new vaccine candidate

Methods for FMD Vaccine Matching

- ***In-vivo* evaluation for cross protection**
  - Requires 30+ days for single immunisation and longer time for revaccination
  - Against animal welfare
  - Expensive
  - Impractical when large volume of samples to be analysed

- **In-vitro analysis**
  - Primary genetic profiling by sequencing
  - Selecting representative field isolates for antigenic matching by serology

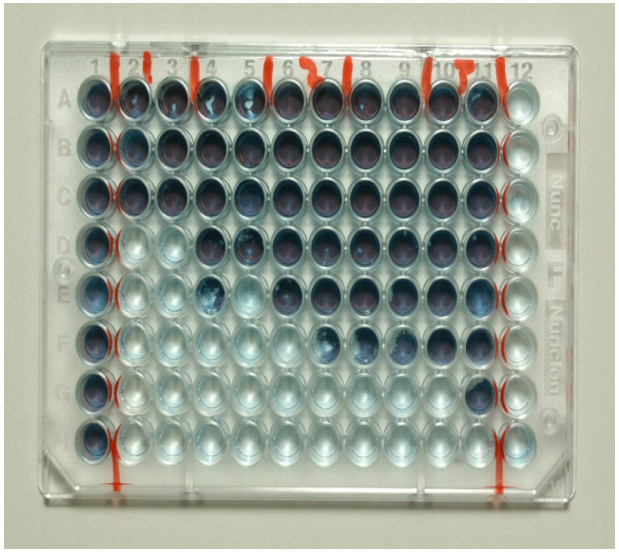
Vaccine Matching by Serology

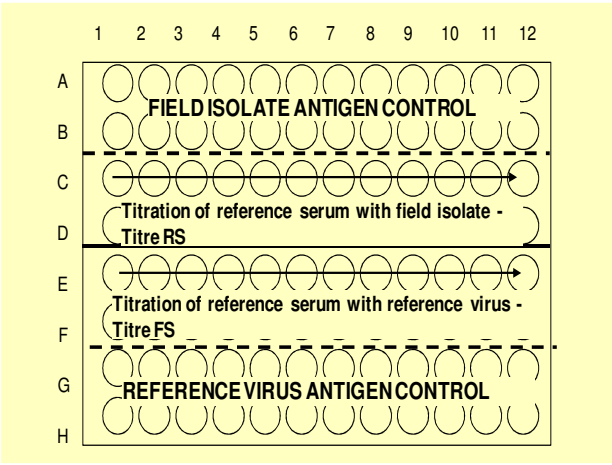
- Measuring the antigenic similarity between the field isolates and vaccine strains by comparing the cross reactivity of a vaccinal serum against these two virus

- The results expressed as

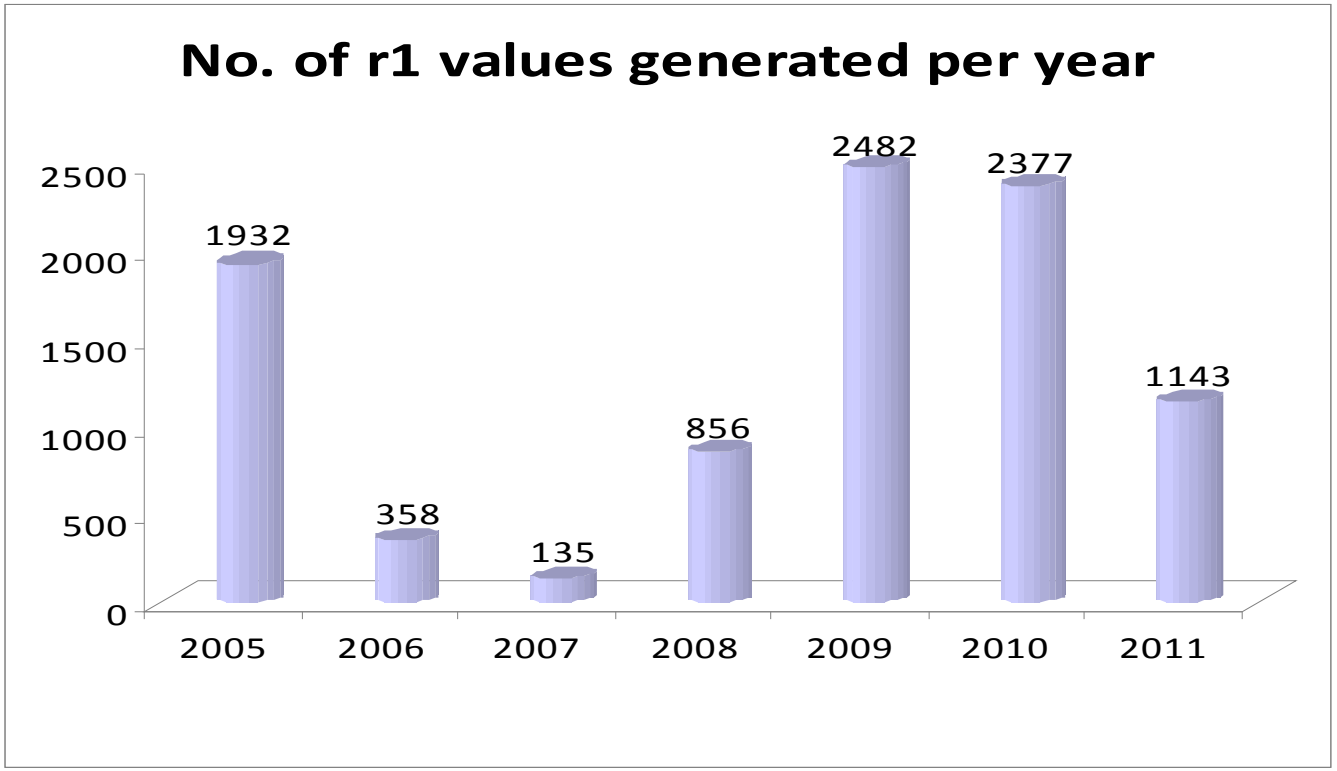
$$r_1 \text{ value} = \frac{\textit{Ab titre of ref. serum against field isolates}}{\textit{Ab titre of ref. serum against vaccine strain}}$$

- Current tests
  - Virus neutralisation test (VNT):72 hours, cut-off: $r_1 \geq 0.3$
  - Liquid phase blocking ELISA (LPBE): two steps: cut-off: $0.2 \leq r_1 < 0.4$; $r_1 \geq 0.4$
  - Complement fixation test (CFT): restricted to S. America

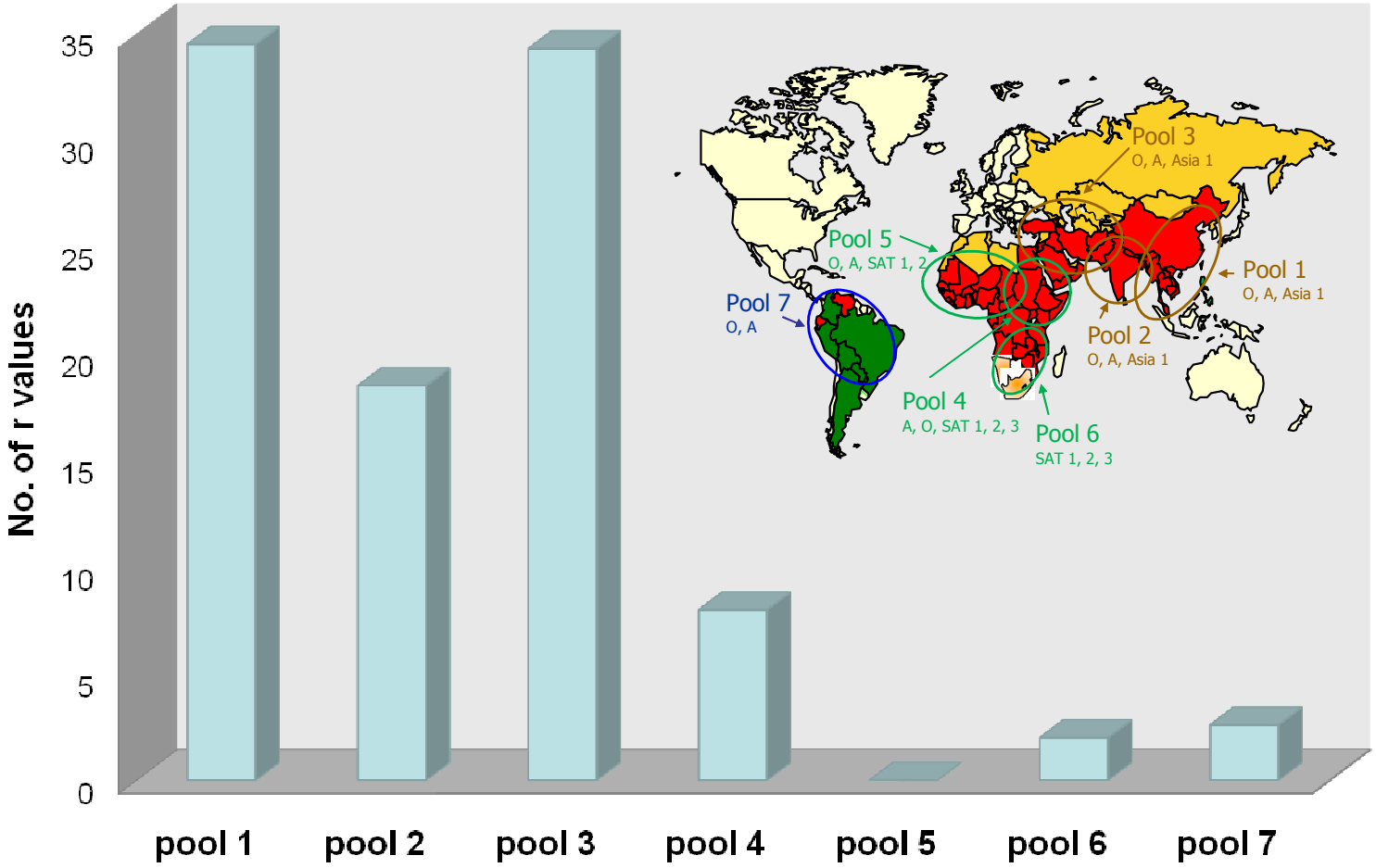




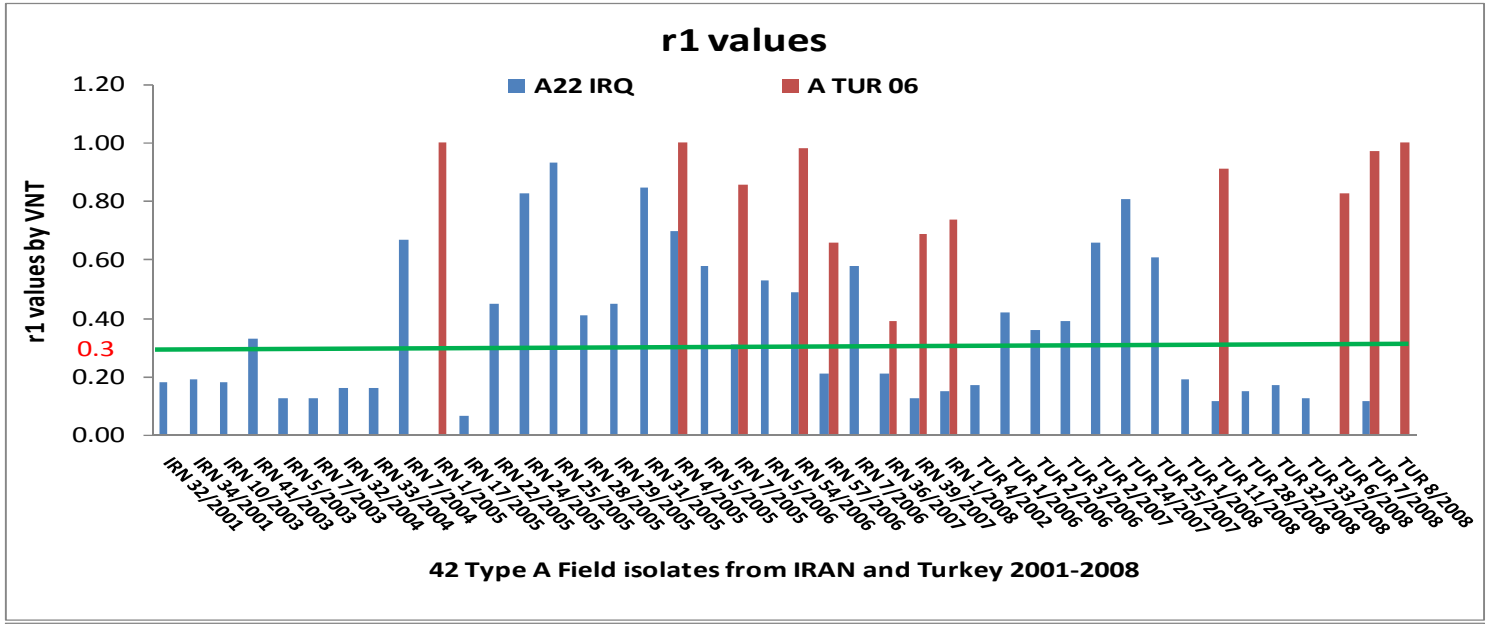
Vaccine Matching by Serology at WRL FMD
--- r_1 values measured by 2dmVNT

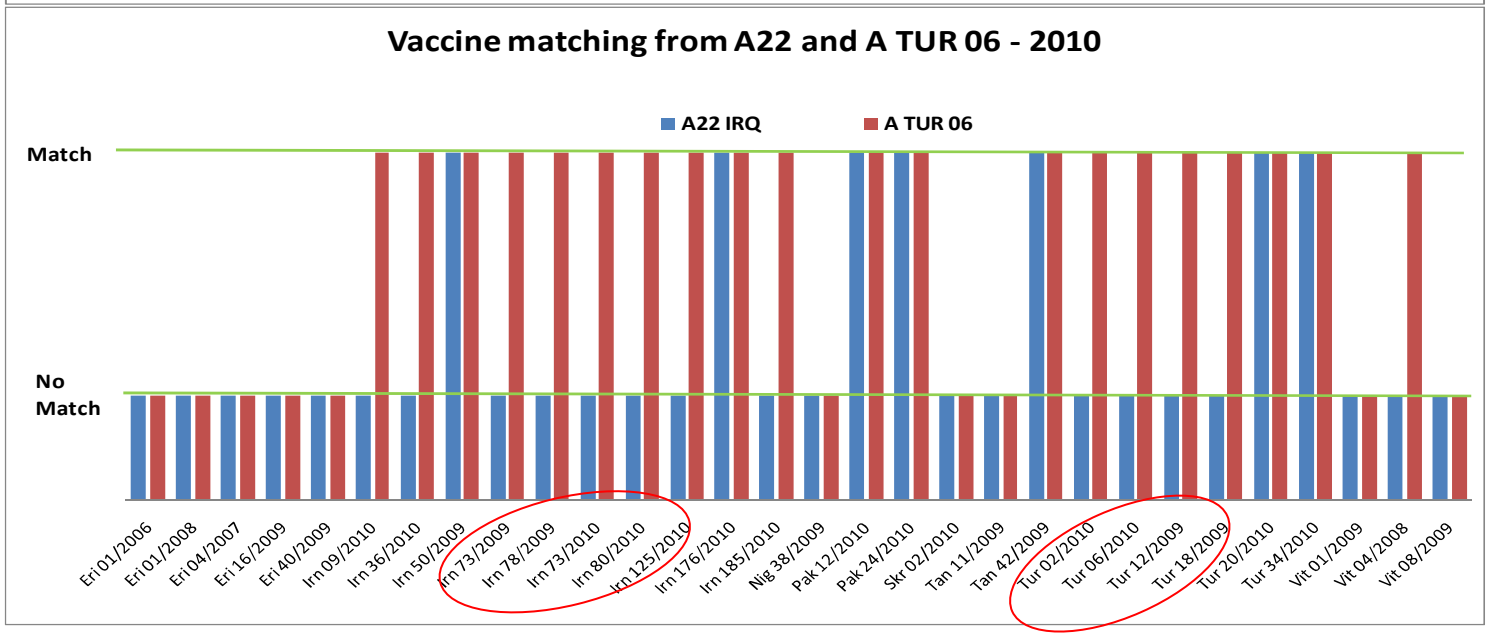


No. of r_1 values Determined Per Pool by WRLFMD During 2011



Emerging of the A IRN 05 Like Virus





ORIGINAL ARTICLE

Recent Spread of a New Strain (A-Iran-05) of Foot-and-Mouth Disease Virus Type A in the Middle East

N. J. Knowles[1], M. H. Nazem Shirazi[2], J. Wadsworth[1], K. G. Swabey[1], J. M. Stirling[1], R. J. Statham[1], Y. Li[1], G. H. Hutchings[1], N. P. Ferris[1], Ü. Parlak[3], F. Özyörük[3], K. J. Sumption[4], D. P. King[1] and D. J. Paton[1]

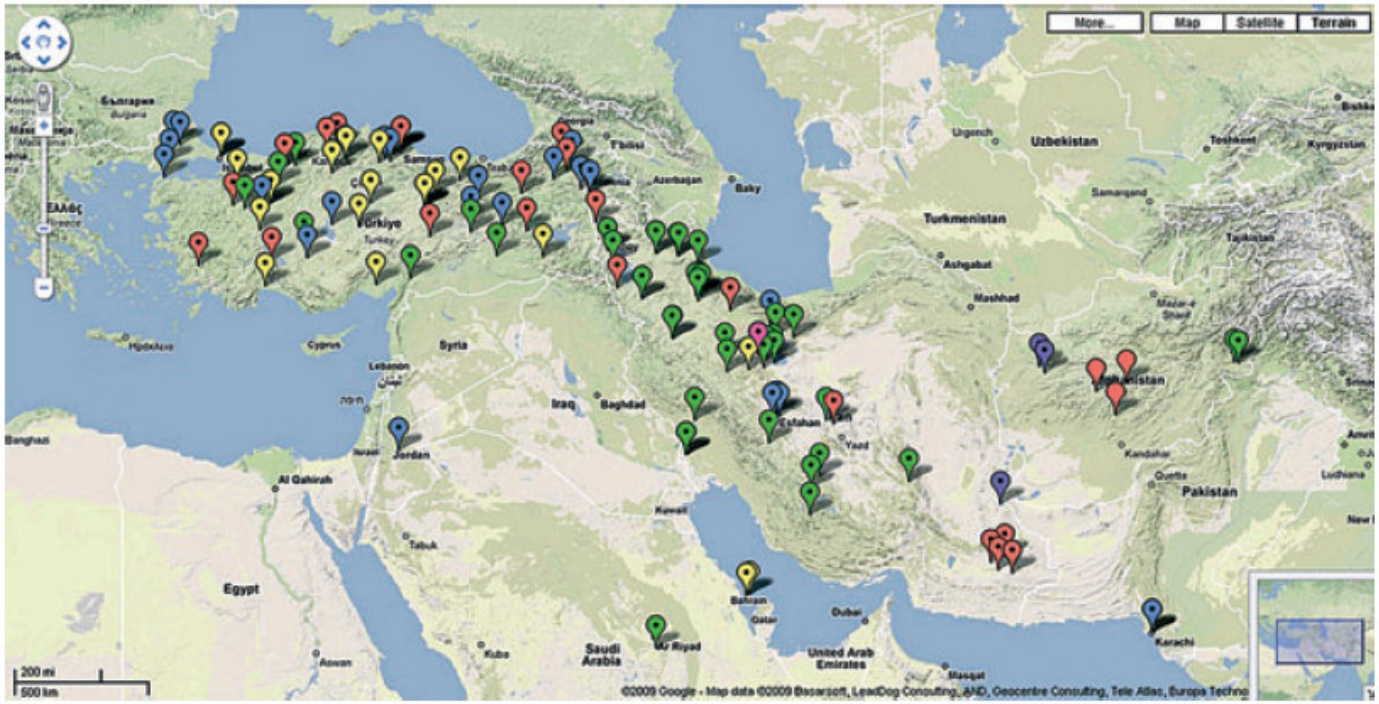
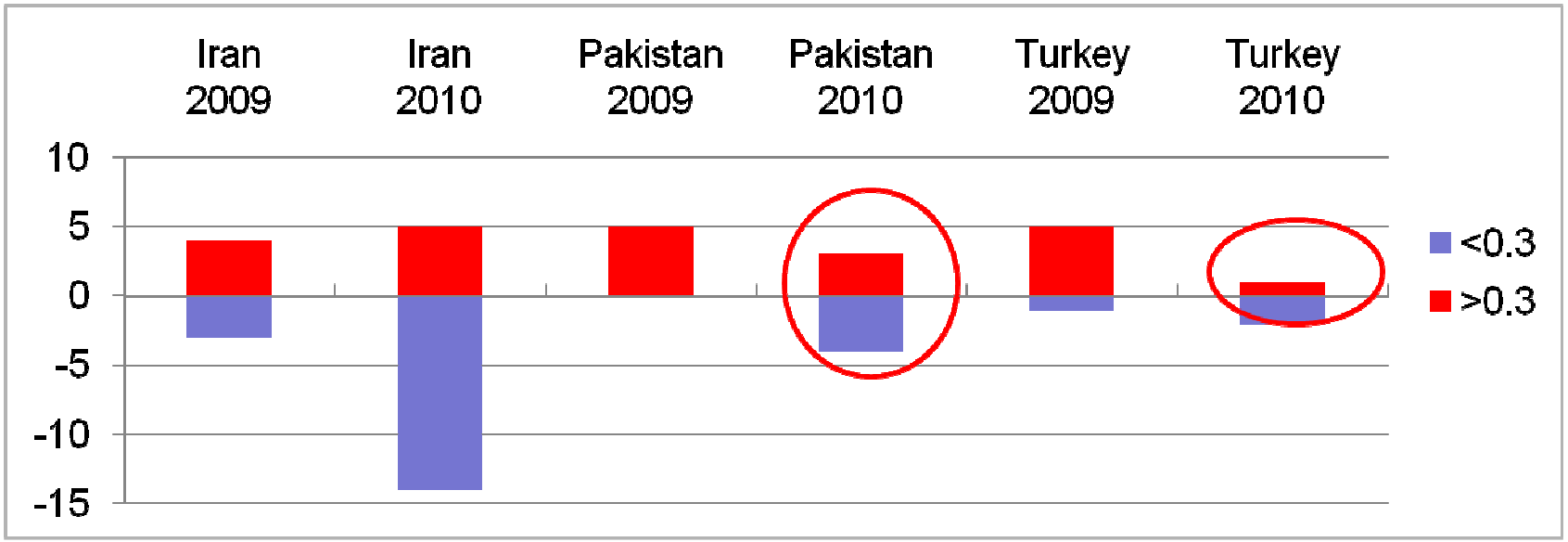
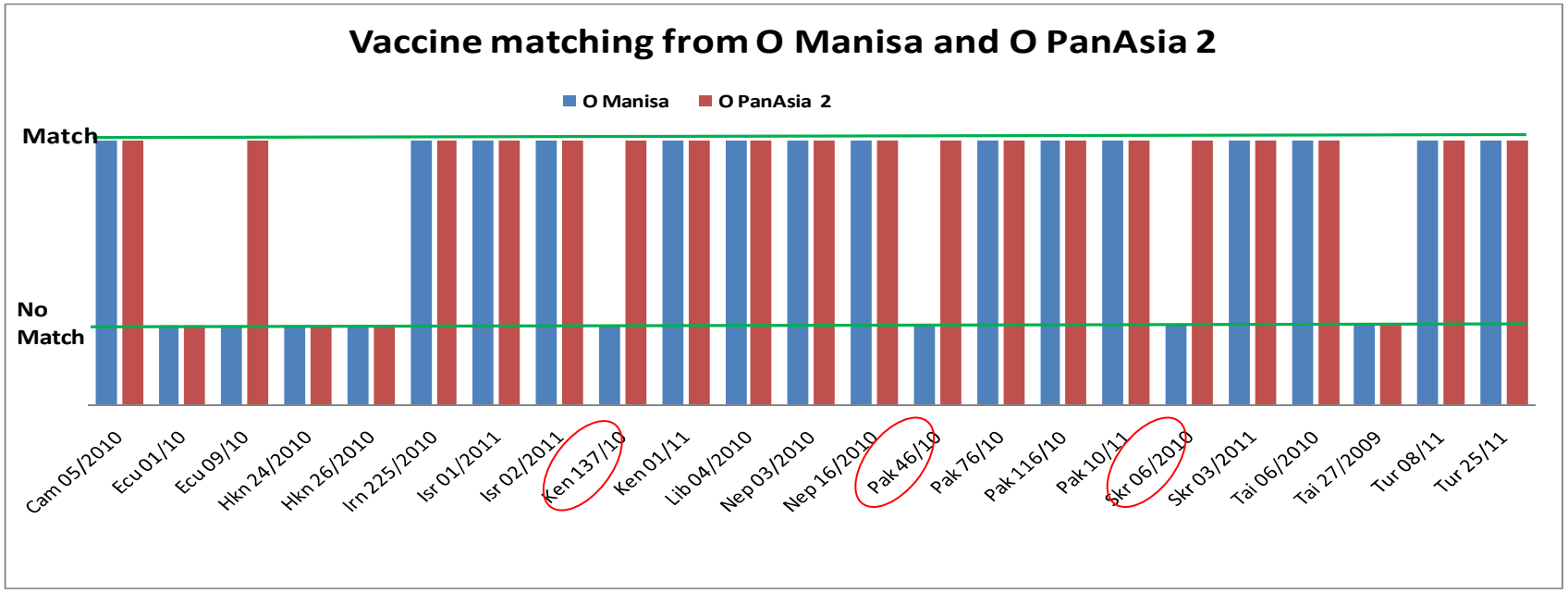


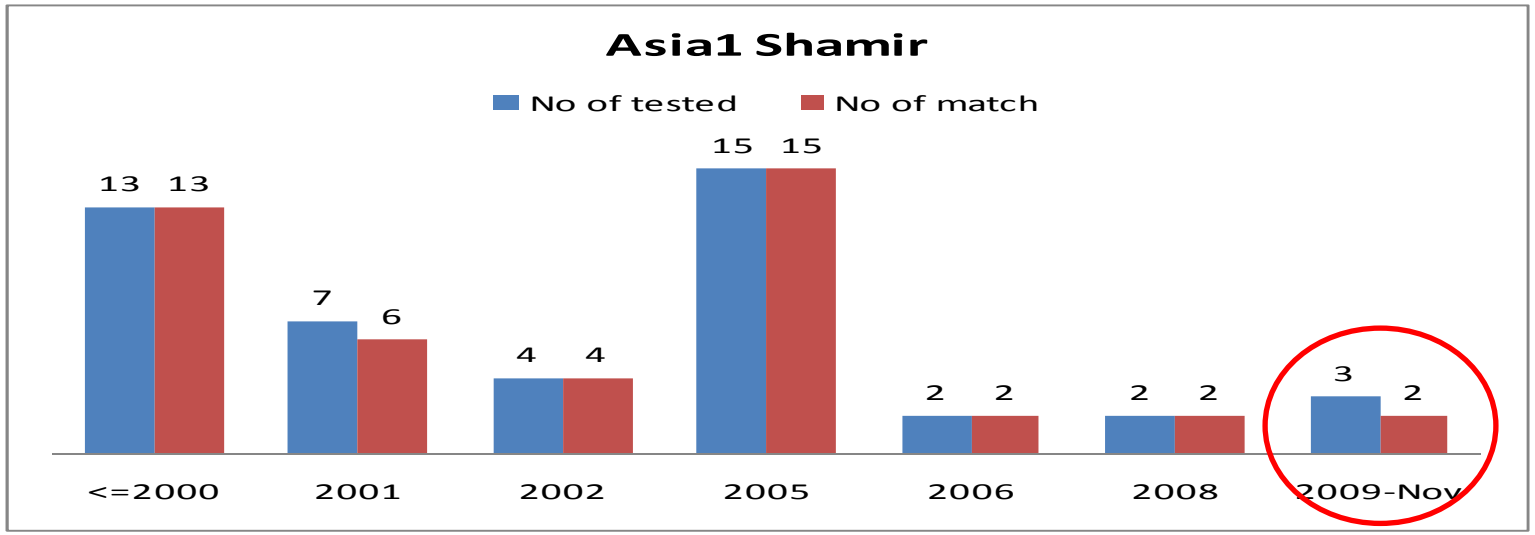
Fig. 2. Map showing the locations of FMDV A-Iran-05 isolates from 2003 to 2008. Pink, 2003; purple, 2004; green, 2005; blue, 2006; red, 2007; yellow, 2008. Those markers that contain a dot indicate known locations while those without are not known and therefore placed in the approximate centre of the country of origin. The map was produced using Google Maps (©Google, 2008).

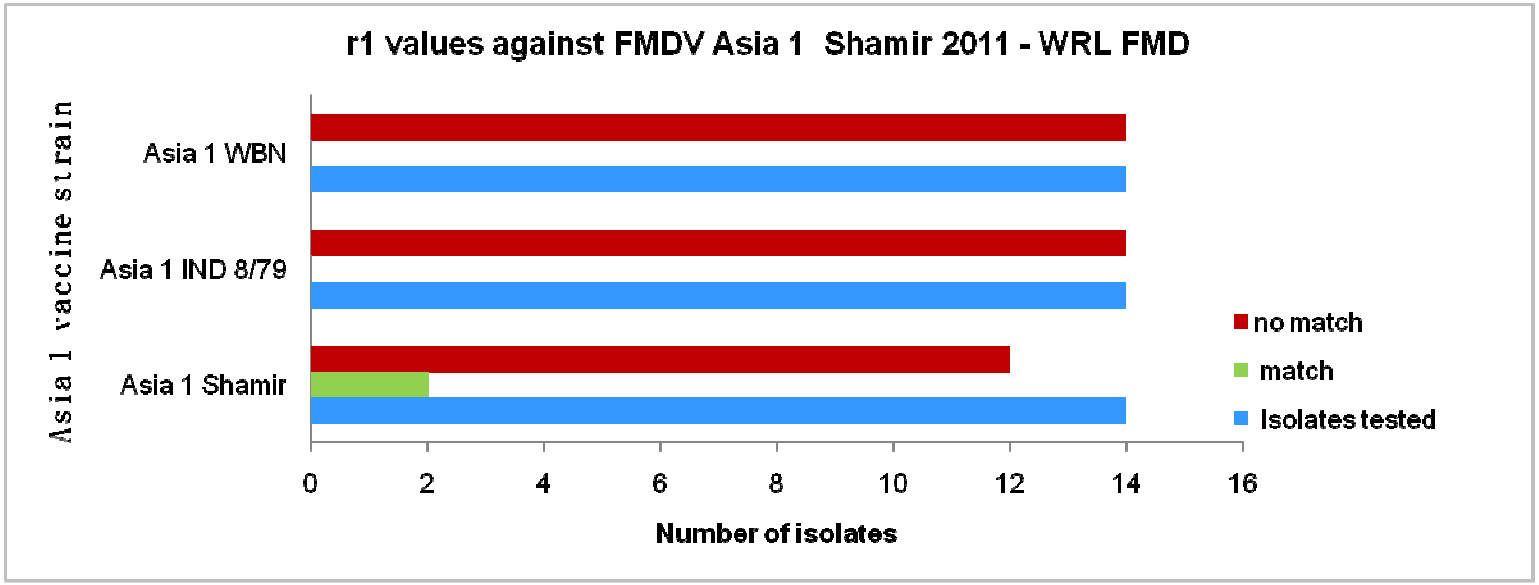
Emerging of O PanAsia 2 Like Virus





Vaccine Matching (type Asia 1) 2000-2009 WRLFMD





Two O_1 Manisa Potency Tests

-Hetrologous challenge with O Iran 34/2006 in Pirbright in 2007

-Homologous challenge with O Manisa in Lelysted in 2008 (Aldo Dekker)

1 dose | 1/4 dose | 1/16 dose | Unvaccinated controls

O Manisa challenge:	4.6 PD50 (Aldo Dekker)
O Iran 34/2006 heterologous challenge:	*3.48 PD50*
r_1 values (mean of four tests):	*0.64*
r_1 for full dose group (mean of five animals):	*0.53*

Asia 1 Shamir Potency Test

Heterologous challenge with Asia 1 TUR 49/2011 in Pirbright in March 2012

1 dose | 1/4 dose | 1/16 dose | Unvaccinated controls

Asia 1 Shamir vaccine >6 PD_{50}

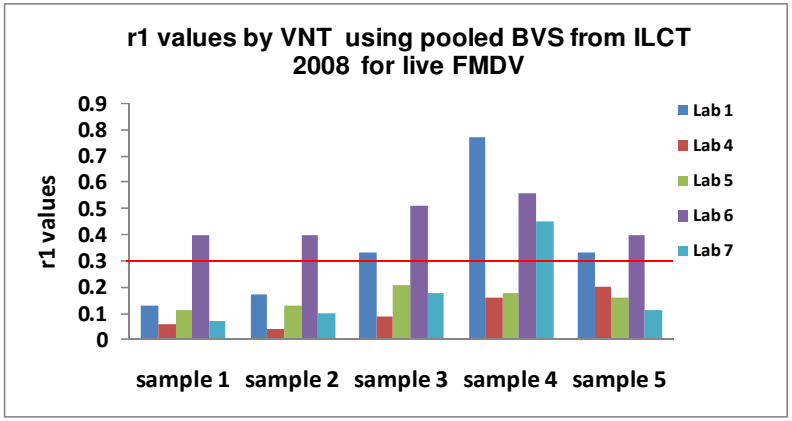
With one inconclusive (culled at 7dpc due to anorexia) gives the vaccine 13.92 PD_{50}

r_1 values (mean of two tests): 0.20

r_1 values and serology testing on experimental samples are under investigation

Issues with Serological Tests

- Available mainly in OIE/FAO ref labs while the most need is the local lab in the origin of the outbreaks
- Results may not be comparable from different labs
  - Variability of reagents
    - vaccine and or/antisera differences
    - reagents for LPB ELISA
    - preparation procedure
  - Variability of tests
    - cells for VNT
    - use of individual or pooled sera
    - protocol differences
  - Lab preference to a test
- Difficult to provide an accurate set of recommendations on vaccine selection for different regions



The 1st OIE/FAO FMD Reference Laboratories Vaccine Matching Technology Training Workshop
Institute for Animal Health, Pirbright,
7-11 November 2011

Future Work to Improve Vaccine Matching for FMD

- Standardization of existing methodologies and FMD vaccine matching training
- Further investigate the relationship between r_1 values and protection efficiency- different potent vaccines and revaccination?
- Use of monoclonal antibodies instead of polyclonal antibodies
- New approaches
  - Capsid sequencing and protein structure modelling based approach
  - Antigenic Cartography

Acknowledgements

SAU, WRL/EURL FMD,

FMD programme,

Aldo Dekker, CIADC, Lelysted

OIE/FAO FMD Ref Lab Network

Defra, EC and FAO-EUFMD

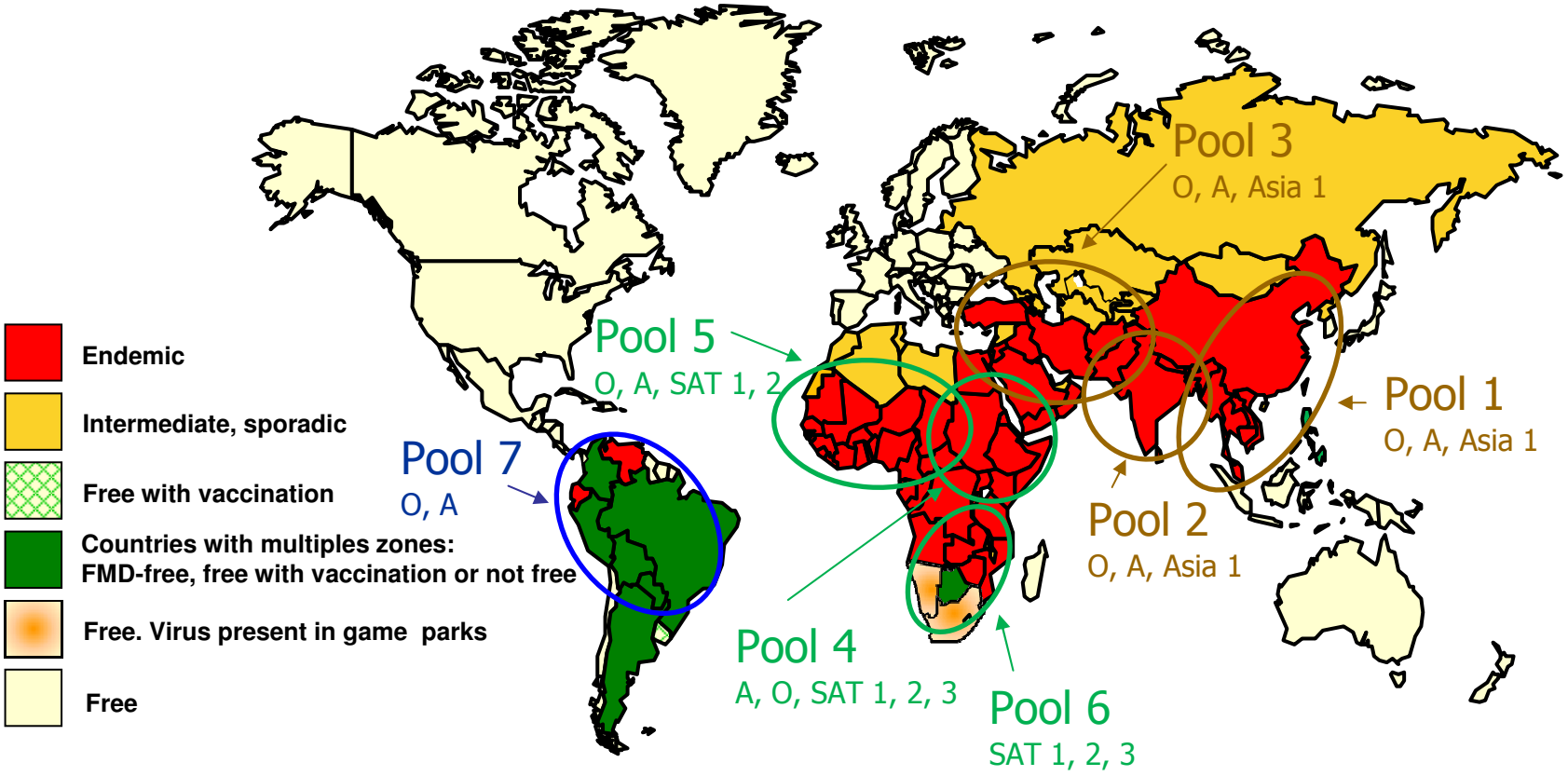
THANK YOU

OVI

WRLFMD

Regional Virus Pools as an Aid to Global Control

- **Divides the globe into 7 virus pools by the OIE/FAO FMD lab network each with**
  - **-Multiple serotypes but topotypes mainly confined to that pool**
  - **-differ in FMDV antigenic, requires tailored vaccines and approach**



Pool positions are approximate and colours indicate that there are three principal pools, two of which can be subdivided into overlapping areas