The Global FMD Situation

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WRLFMD
OIE/FAO Foot-and-Mouth Disease Reference Laboratories Network
THE Pirbright INSTITUTE
BBSRC bioscience for the future
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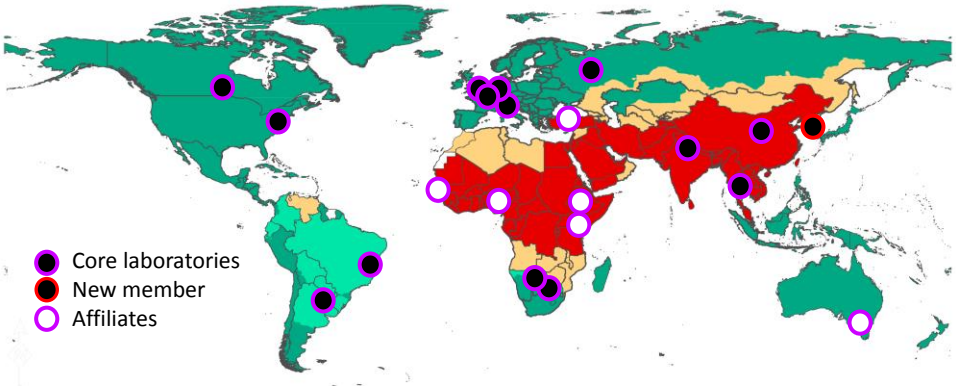
OIE/FAO FMD Laboratory Network

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

- OIE and FAO Reference Centres (+ affiliates)
  - Working Groups (nomenclature and PVM)
  - Meeting reports available http://www.foot-and-mouth.org/
- **Global surveillance and changing patterns in risk pathways**
- **Harmonised and improved lab capacity**



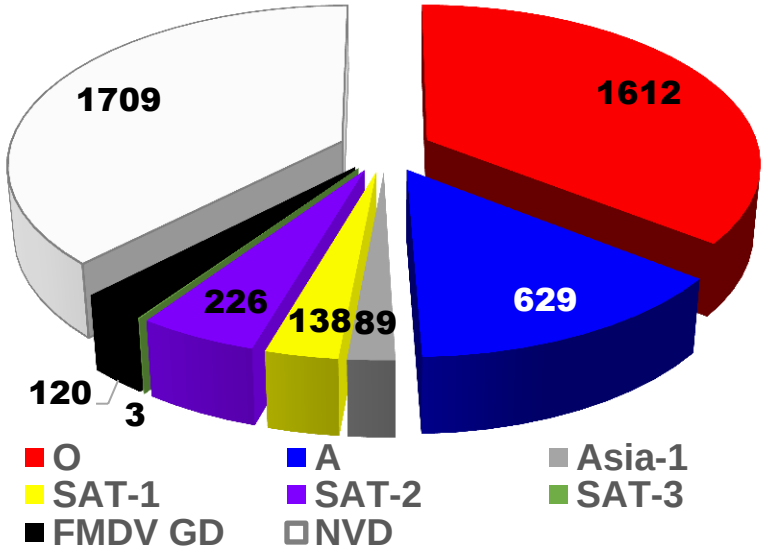
Paris – November 2016

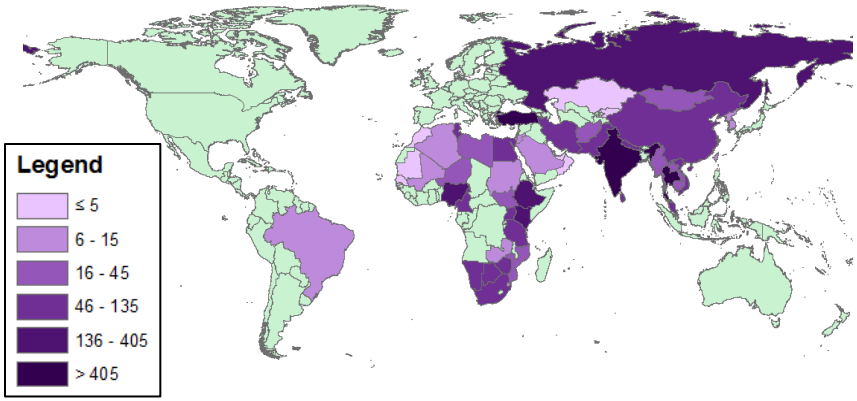
Samples 2014 - 2016

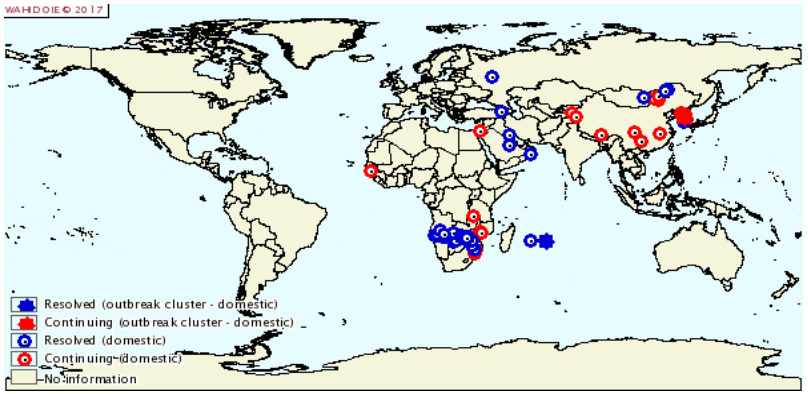
OIE/FAO Network Partners and Affiliates

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

- **4526** samples tested
- **37.7 %** "no virus detected" - NVD
  - Continued attempts to improve local sample collection and more reliable methods for shipment
- Initiatives to improve sample collection/testing in **Pool 4** (East Africa) and **Pool 5** (West Africa)

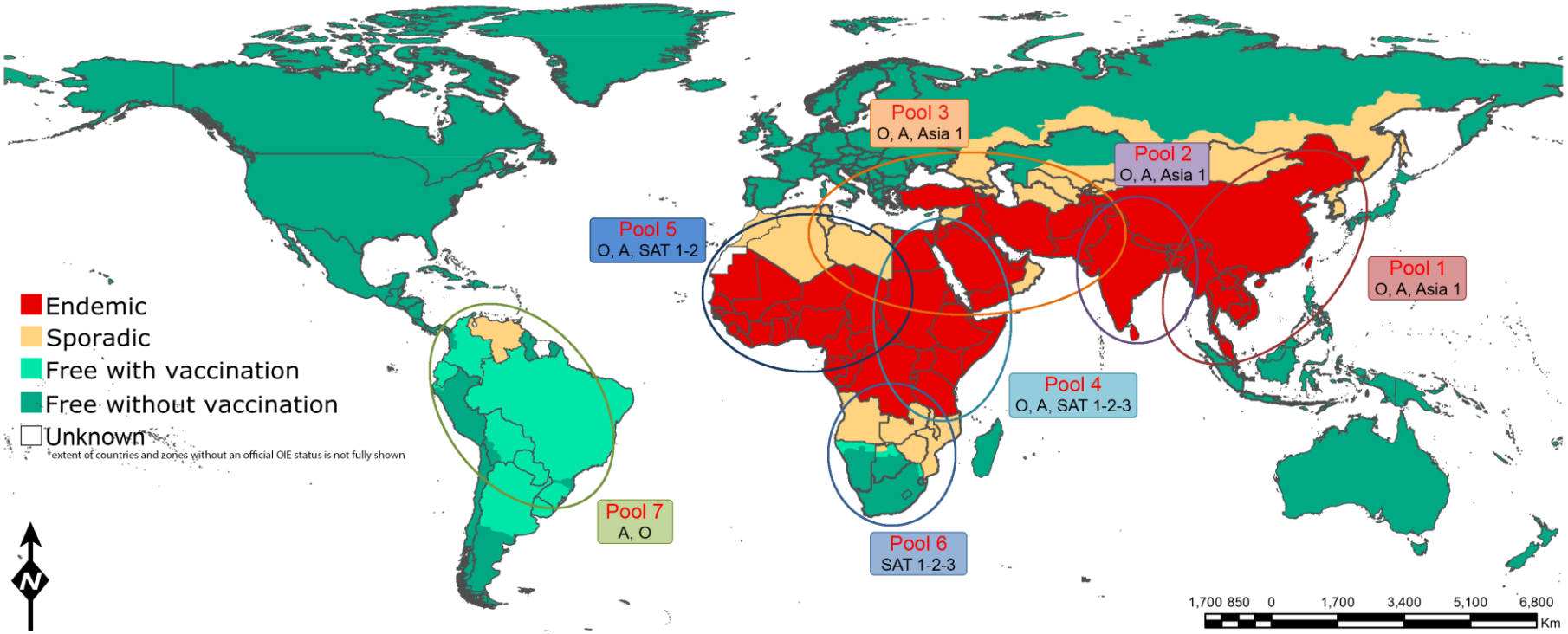






FMD: Summary and conjectured global status

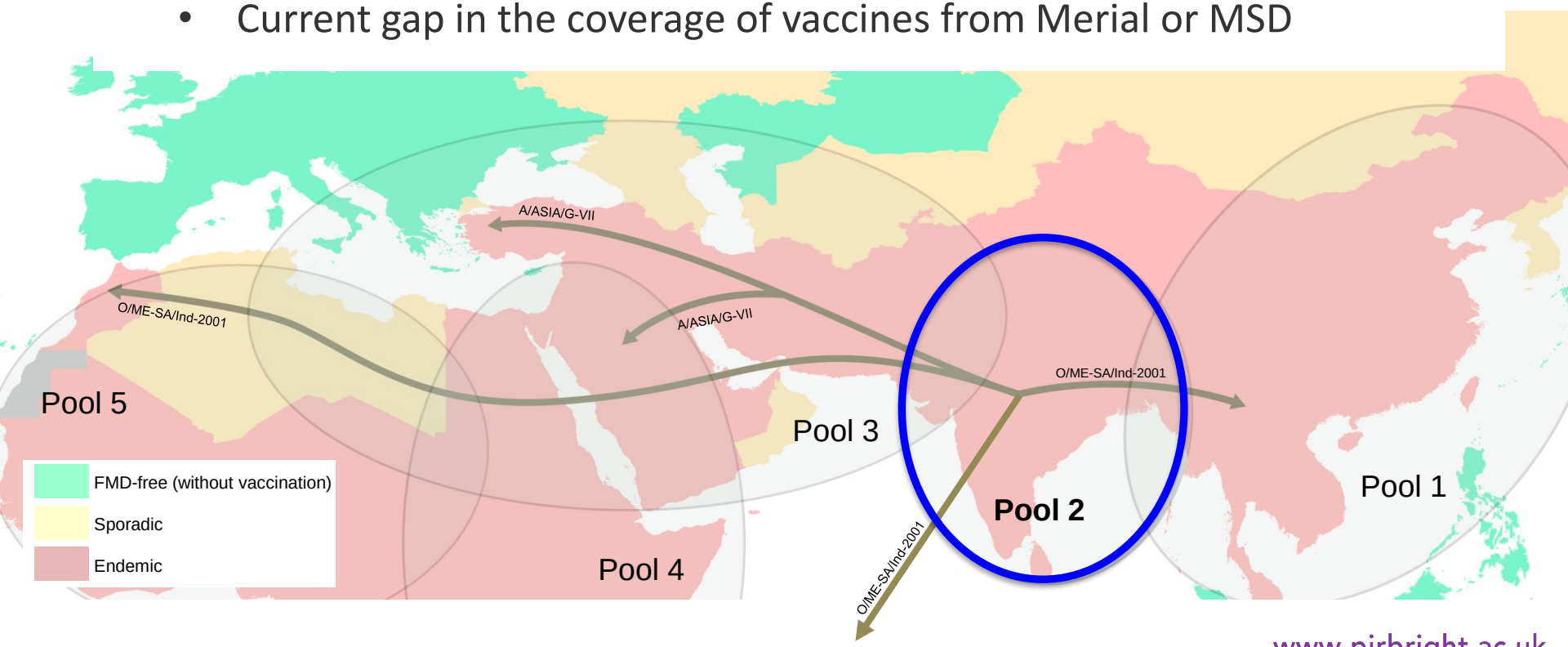
- Seven FMDV serotypes
- **<u>Seven endemic pools</u>** requiring tailored diagnostics and vaccines



- No reported outbreaks in South America since **2013 (Venezuela)**
- No serotype C since 2004
- New FMD-free zone (without vaccination) established in northern Kazakhstan and **Russia (except a new containment zone)**

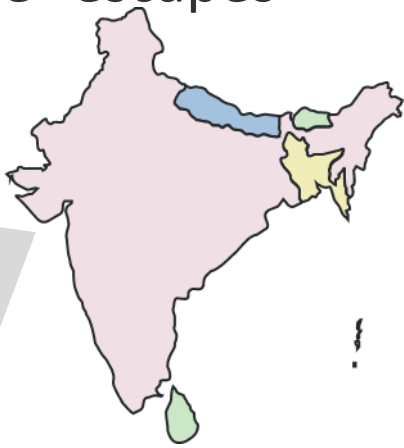
Long-distance “trans-pool” movements from Pool 2

- **O/ME-SA/Ind-2001d**
  - Expanding range of this lineage
  - Data from *in vivo* and field studies regarding suitability of vaccines
- **A/ASIA/G-VII**
  - Emerged in 2015
  - Rapid spread in parts of West EurAsia
  - Current gap in the coverage of vaccines from Merial or MSD



O/ME-SA/Ind-2001d: the new PanAsia?

Sequence data indicates that there have been multiple “escapes” from the Indian sub-continent



Pool 2

Iran (2009)

UAE(2014)

UAE(2015)

North Africa
Tunisia
Algeria
Morocco

2014

Libya

2013

Saudi Arabia (2013)

Bahrain (2015x2)

2014

2013

Sri Lanka

Mauritius (2016)

Pool 1

Laos (2015)

Vietnam (2015)

Thailand (2016)

Myanmar (2016

anses
alimentation, environnement, travail

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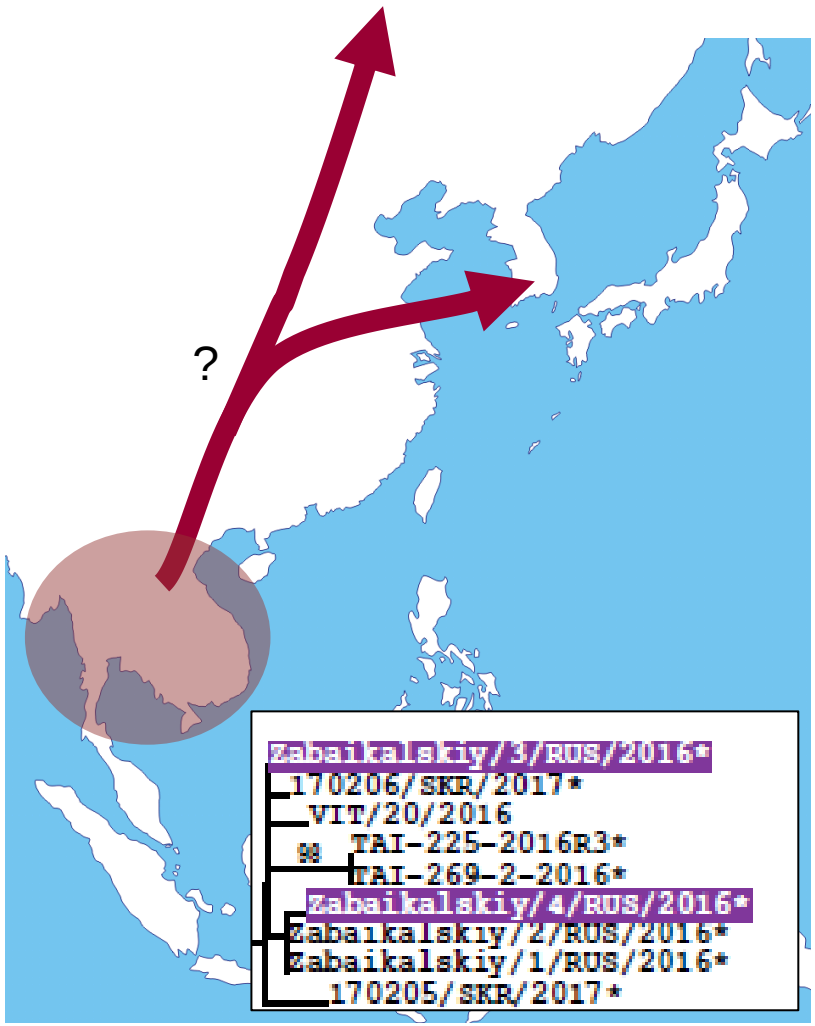
O/ME-SA/Ind-2001d:
Onward transmission from POOL 1?

Russian Federation

- November 2016
- Three outbreaks
- Cattle
- Close to the Chinese border

Republic of Korea

- February 2017
- Eight outbreaks
- Cattle



Can this lineage be found elsewhere in the East Asia region?
Reported yesterday: China (Xinjiang Province)

Vaccine matching for O/ME-SA/Ind-2001

Sample	O 3039	O_1 Manisa	O/TUR/5/2009
ALG/3/2014	0.27	0.13	0.48
BAR/14/2015	0.32	0.13	0.44
BAR/8/2015	0.59	0.22	0.66
BHU/12/2012	0.17	0.12	0.23
BHU/1/2013	0.74	0.17	0.4
LAO/3/2015	0.52	0.18	0.72
LIB/1/2013	0.5	0.13	0.95
LIB/17/2013	0.19	0.12	0.38
LIB/22/2013	0.93	0.38	1.51
LIB/7/2013	0.51	0.16	0.91
MOR/1/2015	0.42	0.27	0.42
MOR/2/2015	0.55	0.32	0.58
MUR/6/2016	0.38	0.65	1
MUR/7/2016	0.35	0.76	0.87
NEP/13/2012	0.51	0.27	0.56
NEP/21/2012	0.24	0.12	0.46
NEP/6/2012	0.36	0.13	0.78
NEP/18/2013	0.4	0.2	0.63
NEP/6/2013	0.36	0.16	0.74
NEP/1/2014	0.37	0.16	0.35
NEP/6/2014	0.63	0.22	1.74
NEP/18/2015	0.54	0.27	0.59
NEP/11/2016	0.47	0.51	0.38
NEP/17/2016	0.41	0.68	0.89
SAU/1/2013	0.45	0.14	0.33
SAU/4/2013	0.63	0.15	0.54
SAU/6/2013	0.5	0.27	0.85
SAU/7/2013	0.54	0.32	1.15
SAU/1/2014	0.28	0.19	0.79
SAU/1/2016	0.89	0.39	0.89
SAU/7/2016	0.32	0.35	0.48
SRL/1/2013	0.46	0.23	0.76
SRL/1/2014	0.48	0.29	0.85
SRL/28/2014	0.58	0.25	0.42
SRL/30/2014	0.43	0.23	0.15
TUN/1/2014	0.26	0.11	0.52
UAE/1/2014	0.25	0.3	1.74
UAE/2/2014	0.42	0.27	1.1
UAE/1/2015	0.66	0.43	0.87
UAE/2/2016	0.55	0.34	0.55
VIT/8/2015	0.71	0.58	0.52
VIT/20/2016	0.66	0.56	0.66

42 field isolates

Using VNT r-value 0.3 cut-off

Not Matched	r-value is <0.28
Borderline	r-value is between 0.28 and 0.32
Matched	r-value is >0.32

Vaccine Potency Trial

O/ME-SA/Ind2001d

- Experiments hosted by CVI-Lelystad
- Adopted protocol according to European Pharmacopeia
- O-Manisa vaccination (at least $6PD_{50}$) with O/ALG/2014 challenge

Vaccine Dose	Number Protected vs Vaccinated	Serological Results (O Manisa Log_{10} VNT mean 21DPV)
Full	3/5	2.65
1/4	4/5	2.67
1/16	0/5	1.68
Unvaccinated*	0/2	

- Estimated heterologous potency ~3 PD_{50}

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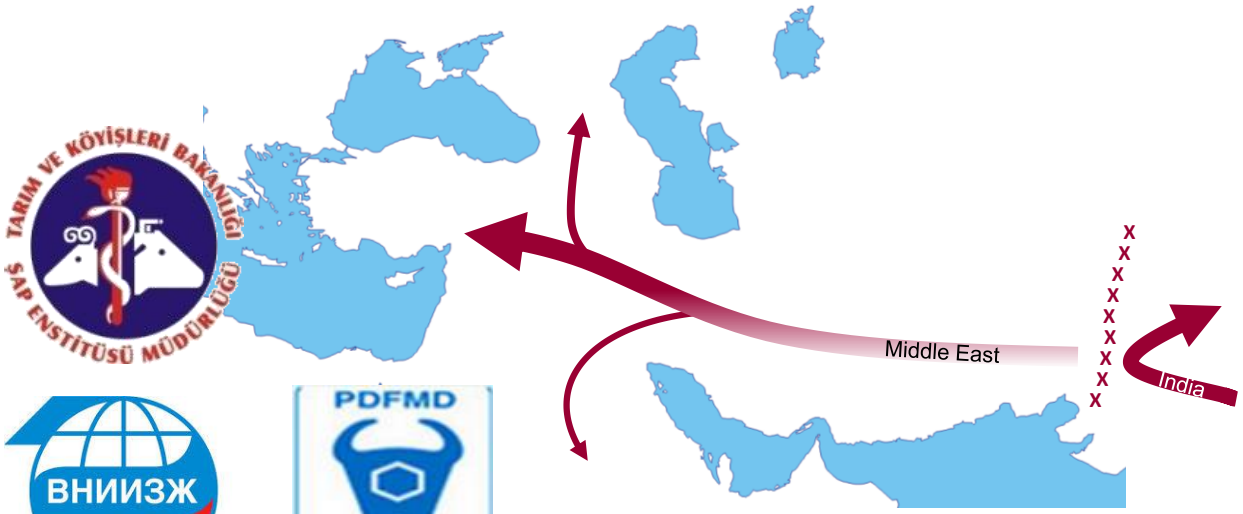
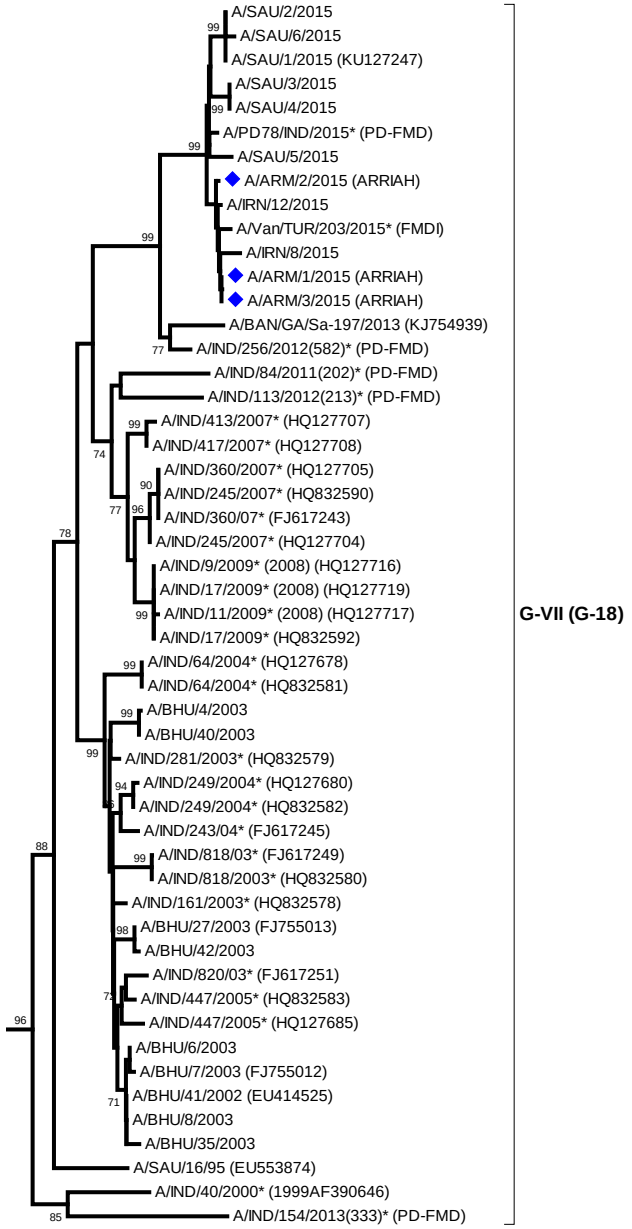
WAGENINGEN UR For quality of life

Other data for O-3039 and O-Manisa vaccine presented by Singanallur at EuFMD

New serotype A outbreaks in West EurAsia (A/ASIA/G-VII)

- Initial reports September 2015
- **Saudi Arabia, Turkey, Iran, Armenia**
- Originating from the Indian sub-continent
- Impact upon vaccination?





A/ASIA/G-VII

Poor *in vitro* match to many commercial vaccines

Recent r-values:

Vaccines	A/SAU/1/2015	A/SAU/2/2015	A/IRN/8/2015	A/IRN/12/2015	A/IRN/25/2015
A-Iran-05	0	0	0	0	0
A-Tur-20-06	0.03	0.06	0.01	0.15	0.01
A-22	0.11	0.11	0.13	nd	0
A-Iran-87	0	0.04	nd	nd	nd
A-Iran-96	0.04	0.06	nd	nd	nd
A-Iran-99	0.01	0.01	nd	nd	nd
A-Sau-95*	0.20	0.19	0.26	0.16	nd
A-May-97	0.14	0.23	0.15	0.23	nd
A-Tur-11	0.01	nd	0.10	0.04	nd
A-Tur-14	0	nd	0	0	nd
A-IND-40-2000*	0.26	nd	0.03	0.24	nd

* Multiple BVS tested

A/ASIA/G-VII (G18) – vaccine trial

- Monovalent vaccines were not immediately available from Merial
- Polyvalent vaccine
  - O-3039, O-Manisa, O-PanAsia-2, A-Iran-05, **A-Sau-95**, Asia-1, SAT 2
- PPG format in cattle
- Challenge at 21 dpv with A/IRN/2015

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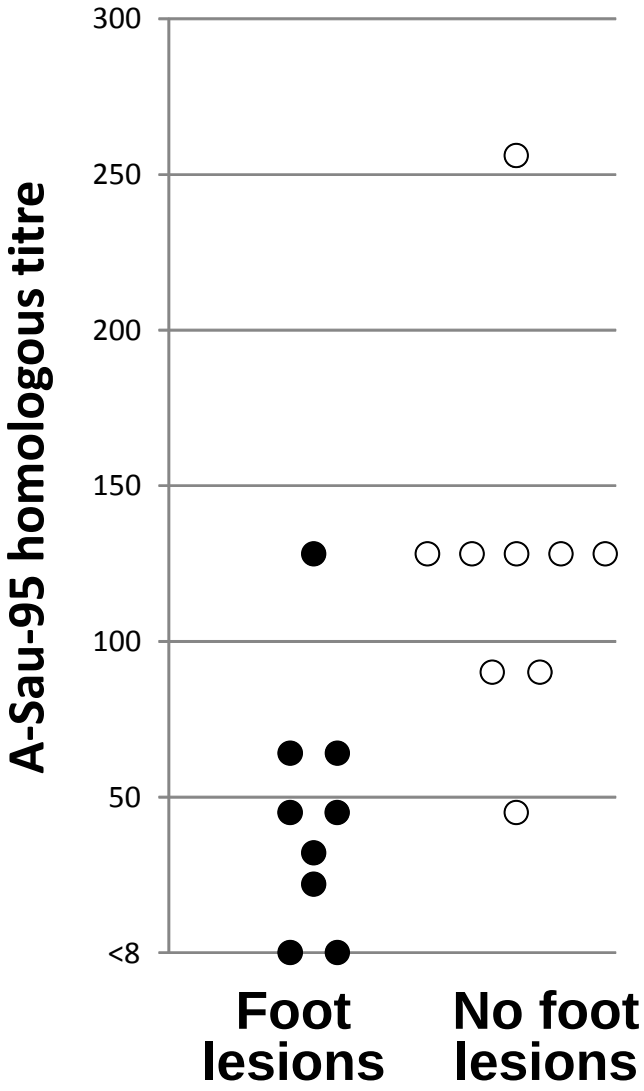
TPI Vaccine trial (summary of results)

- Both control animals developed foot lesions
- 7/16 vaccinates developed foot lesions
- Only **56% protection** from generalisation
- A-Sau-95 titres (measured by VNT) correlated with protection

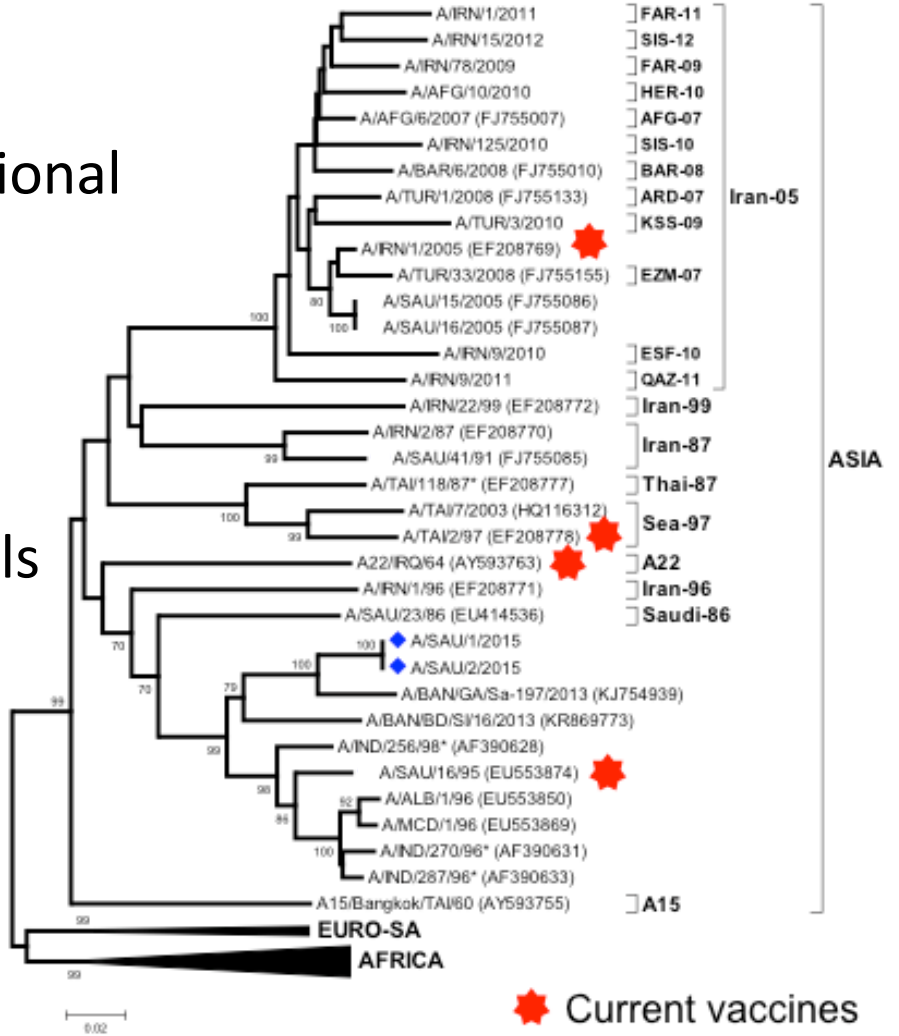
- Use of vaccine in endemic settings where animals are multiply-vaccinated



A/ASIA/G-VII (G18)

Additional vaccine trial

- December 2016
- Pilot trial to evaluate two additional FMDV vaccines (from Merial)
  - A22
  - A/May-97
- Single groups of cattle
  - 7 for each vaccine, 3 controls
- Preliminary data:
- A22 – 2/7 protected
- **A/MAY/97 – 5/7 protected**



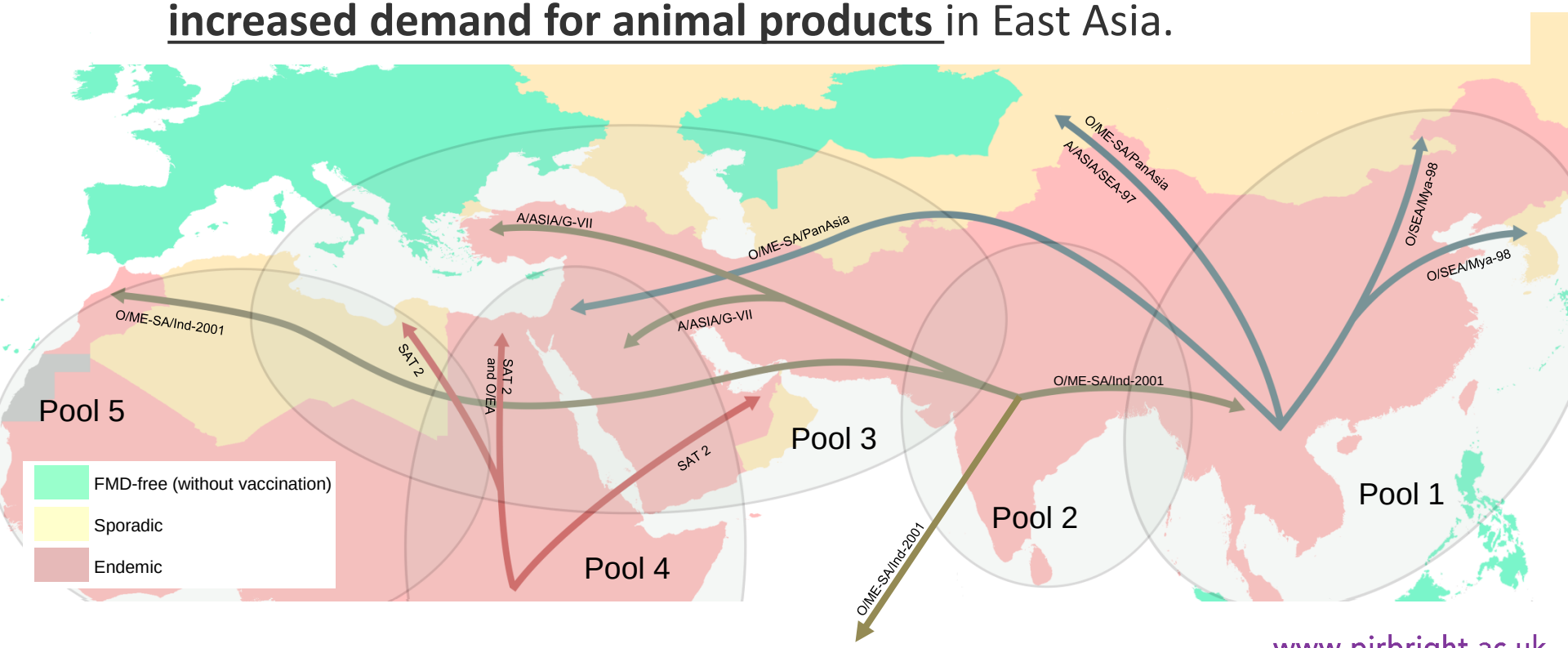
Summary
O/ME-SA/Ind-2001d and A/ASIA/G-VII

- Long distance movements
  - Important role of the **Indian sub-continent** as a source
  - Do we understand these connections?
- **O/ME-SA/Ind-2001d lineage**
  - Good evidence from *in vivo* studies and field studies that vaccines provide appropriate heterologous responses
- **A/ASIA/G-VII lineage**
  - Now a threat for SEA? – similar to O/ME-SA/Ind-2001d
  - Impact of existing natural and vaccine immunity to A/ASIA/Sea-97?
  - Surveillance is required
  - **Current gap and vulnerability for emergency vaccination in FMD-free countries (until 2017?)**

Long-distance “trans-pool” movements

Why now?

- Probably no single factor that underpins these dynamic transboundary patterns;
- although these long distance and rapid movements of FMDV are probably exacerbated by the **escalation of regional political crises**, and **migration of people** in North Africa and the Middle East and **increased demand for animal products** in East Asia.



Pool 1:

Characterisation of different FMD virus lineages

2017: based on data from the OIE/FAO Lab Network

Country	O					A		Asia-1
	ME-SA/Ind-2001d	SEA / Mya-98	CATHAY	ME-SA / PanAsia	ME-SA/PanAsia-2	ASIA / Sea-97	ASIA/Ind	
Cambodia		2014		2015		2015		
Laos	2015	2016		2012		2015		
Malaysia		2016			2006	2014		
Myanmar	2016	2016				2015	2010	2005
Thailand	2016	2016	2012	2015		2016		
Vietnam	2016	2016	2016	2014		2016		2006

Is this the true picture of FMD in SEA?

……. or does under-sampling bias our understanding of the epidemiology of the disease?

Vaccine Matching (2015 – 2017)

Serotype O

			O 3039	O_1 Manisa	O/TUR/5/2009	O SKR
CATHAY	-	HKN/1/2015			0.02	
		HKN/2/2015		0.06	0.02	
		HKN/8/2015	0.25	0.09	0.17	0
		HKN/9/2015	0.16	0.06	0.12	0
		HKN/3/2016	0.10	0.13	0.11	0.03
		HKN/5/2016	0.06	0.15	0.14	0.04
		VIT/8/2016	0.13	0.18	0.16	
ME-SA	Ind-2001	LAO/3/2015	0.52	0.18	0.72	0.63
		VIT/8/2015	0.71	0.58	0.52	
		VIT/20/2016	0.66	0.56	0.66	
	Pan Asia	CAM/03/2015	0.55	0.2	0.65	0.62
		TAI/16/2015	0.89	0.36	0.65	
SEA	Mya-98	MAY/1/2015	0.33	0.35	0.50	
		MOG/02/2015	0.72	0.25	1.29	
		MOG/04/2015	0.51	0.23	1	
		MYA/01/2015	0.16	0.05	0.19	0.01
		MYA/05/2015	0.34	0.21	0.74	0.34
		TAI/09/2015	0.66	0.32	0.44	
		TAI/26/2015	0.65	0.32	0.74	
		MAY/10/2016	0.69	0.45	1.00	
		MAY/5/2016	0.68	0.60	0.69	
		SKR/07/2016	0.50	0.19	0.47	0.49
		TAI/02/2016	0.68	0.23	0.69	
		TAI/26/2016	0.41	0.18	0.28	
		TAI/37/2016	0.39	0.22	0.43	
		VIT/17/2016	0.25	0.23	0.27	

Vaccine Matching (2015 – 2017)

Serotype A

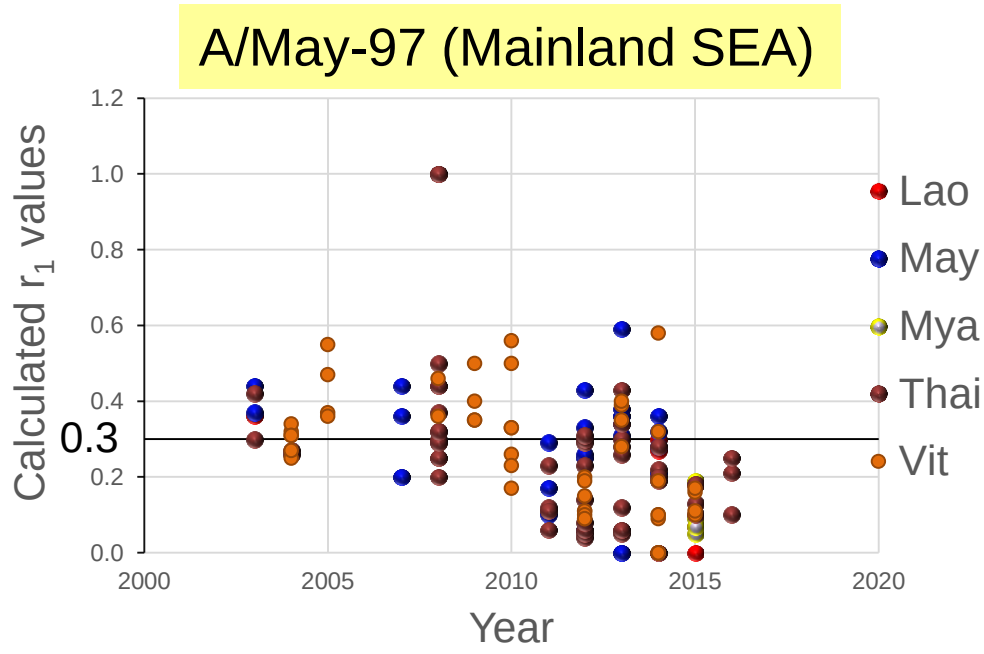
ASIA /Sea-97	A/IRN/05	A/TUR/20/06	A22/IRQ	A/MAY/97
LAO/1/2015	0.33	0.04	0.39	0.11
TAI/1/2015	0.60	0.17	0.50	0.15
TAI/15/2015	0.00	0.01	0.22	
TAI/24/2015	0.40	0.01	0.31	
TAI/4/2015	0.35	0.08	0.38	0.13
VIT/10/2015	0.12	0.15	0.50	0.48
VIT/2/2015		0.18	0.26	0.13
VIT/3/2015	0.09	0.02	0.17	0.14
TAI/20/2016	0.13	0.11	0.26	0.23
TAI/23/2016	0.62	0.10	0.91	0.14
TAI/7/2016	0.54	0.06	0.30	
TAI/8/2016	0.50	0.01	0.36	
VIT/1/2016	0.52	0.14	1.00	0.15
CAM/2/2015	0.54	0.13	0.24	0.43
CAM/5/2015	0.32	0.12	0.28	0.30
MYA/2/2015	0.50	0.22	0.89	0.06
MYA/3/2015	0.42	0.12	0.71	0.05

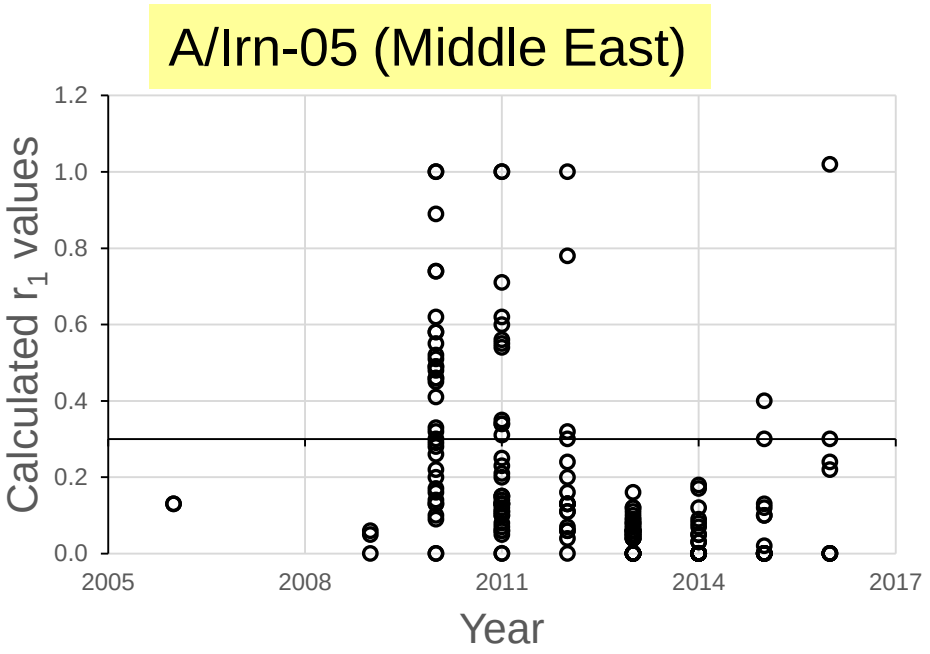
Predictive – for A22: Proline RGD+3

Summary of vaccine evaluation data

	A May 97		A22 Iraq		
Species	Cattle		Cattle		Sheep
Challenged at	21 dpv	7 dpv	21 dpv	7 dpv	4 dpv
Route	IDL	IDL	IDL	IDL	Direct Contact
Protection	100%	60%	100%	80%	83%
NSP Ab	Yes	Yes	Yes	Yes	Yes
Carriers	Yes	Yes	Yes	Yes	Yes
Virus in nasal and oral swabs	Yes	Yes	Yes	Yes	Yes

- High potency serotype A vaccines provide protection from clinical disease against heterologous challenge
- Challenge with A/VIT/15/2012





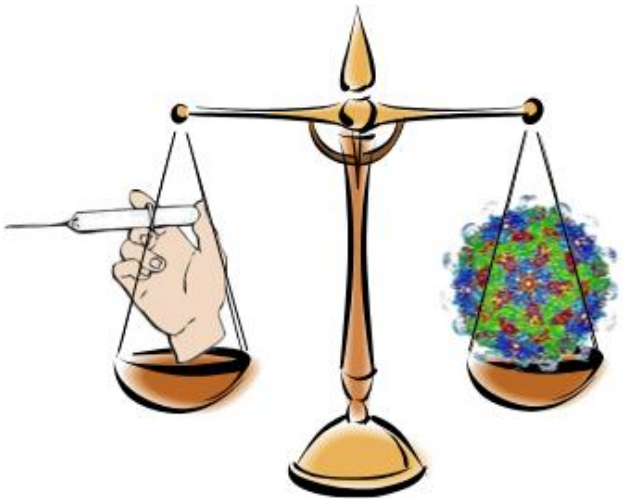
Understanding the factors that influence *in-vitro* vaccine matching for Malaysian strains of FMDV

Lack of reproducibility in vaccine matching tests is caused by reagent related factors; particularly the quality and variability of the:

- cell cycle
- bovine vaccinal sera (BVS)
- antigens

FMDV vaccines

Coordination of different tools that are available?



In-vitro vaccine matching

Pilot Field trials

In-vivo potency cross-protection

Vaccine effectiveness studies

ASSESSMENT of PROTECTION

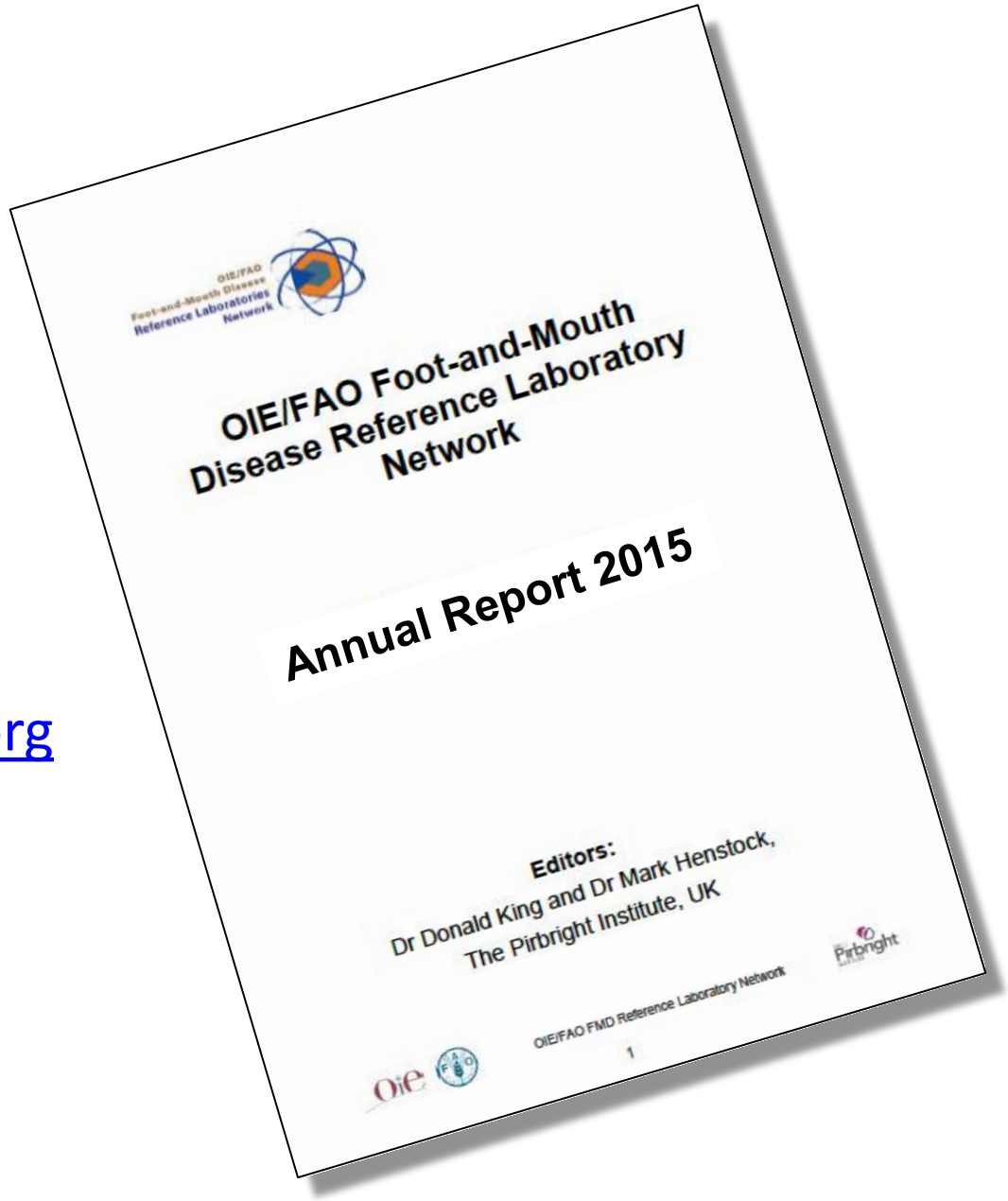
COST and TIME

Summary

- Since 2010 – increased trans-pool movements of FMDV
- At least one new FMDV lineage has entered SEA/East Asia (O/ME-SA/Ind-2001d)
- **Other new threats (A/ASIA/G-VII)**
- FMD viruses from SEA (Pool 1) have caused outbreaks across an number of East Asian countries (e.g., China, Mongolia, Republic of Korea, Russia)

- Vaccine evaluation only starts with vaccine matching
- Pilot studies and field studies are important to demonstrate the vaccines are efficacious

Network report:



- www.wrlfmd.org
- www.foot-and-mouth.org

- Contributions and suggestions welcome

Acknowledgements

- Support for the WRLFMD and research projects
- Collaborating FMD Reference Laboratories and field teams
- Partners within the OIE/FAO FMD Lab Network

Department for Environment Food & Rural Affairs

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