David Paton, Yanmin Li and John Bashiruddin on behalf of all the network colleagues

OIE/WAVLD, Madrid, 19th June 2009
Presentation overview

- Background to formation of the Network
- Network constitution and achievements
- Future direction
The Need for a FMD Ref Lab Network

• Making available accurate and timely global surveillance information
  – Value of sharing information on transboundary diseases, despite pressures against transparency
  – Developing trust and shared vision through ongoing contact and joint programmes of work

• Network goals
  – Understanding global FMD virus distribution and patterns in order to identify threats and make vaccine recommendations
  – Improving the quality of laboratory tests from international and national reference laboratories
  – Building up local capability in support of regional control programmes
Origins of the FMD Ref Lab Network

- OIE Ad Hoc Group on Antigen and Vaccine Banks for FMD (1\textsuperscript{st} Meeting, Paris, 23-25 June 2004)

- Recognised need for two networks with synergistic activities
  - Ref Lab Network to identify vaccine strain priorities
  - Vaccine Bank Network to help make emergency vaccines available

- EU Coordinated Action on FMD and CSF (1\textsuperscript{st} Jan 2005 - 30\textsuperscript{th} June 2008) – provided facilitation and funding
Future development and operation of a potential vaccine bank network

- An international FMDV vaccine/antigen bank network would be beneficial in many ways
  - Exchange of technical know-how and information on strain selection and performance
  - Access to the vaccines/antigens in other banks could reduce the burden of stockpiling on individual members and increase the range of strains available

- Nevertheless, the administrative challenges to making this a reality are formidable
  - Constraints related to confidentiality, disparate standards, conflicts of interest and complex administration
Reference Laboratories and Collaborating Centres

- EAH-ARC, ZA
- CODA-CERVA, BE
- FADDL, US
- FGI-ARRIAH, RU
- IAH, UK
- LFA, AR
- LVRI, CN
- PANAFTOSA, BR
- RRL, TH
- RRLSS, BW
- ICAR, IN
- EAH-ARC, ZA

Reference Centres

Regional/National Reference Centres
Sharing information

• Annual meetings
  – Pirbright 2005
  – Florianopolis 2006
  – Gaborone 2007
  – Lanzhou 2008
  – Delhi 2009

• Annual Reports to OIE/FAO

• Joint publications

• Memorandum of understanding

• Web-based information portal (ReLaIS)

• Inter-laboratory comparative vaccine matching trials
Annual Report

- Unique collation of data and interpretation
- Maps to show distribution of outbreaks and origins of samples submitted to Network Labs
- Delineation of regional viral pools
- Changes in status
- Gap analysis
- Threats
- Vaccine recommendations
- Tables of detailed laboratory results: serotyping, genetic comparisons and vaccine matching tests
FMD outbreaks reported to FAO/OIE during 2008 and identified at country level (although some may be highly localised)

- Bahrain: O, A
- Kuwait: O, A
- Bhutan: untyped
- Israel
- Lebanon
- Malaysia: GD
- Kenya: O, SAT1, SAT2
- Ethiopia: O, A, SAT1, SAT2
- Senegal: GD
- Bahrain: O
- Kuwait: A
- Senegal: SAT 1
- Lebanon: SAT 2
- Bahrain: Asia 1

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FMD outbreaks reported to FAO/OIE during 2008 and identified at country level (although some may be highly localised)
Countries submitting samples to the Network Laboratories for FMD diagnosis in 2008

- Lebanon
- Kuwait
- Israel
- Bhutan
- Bahrain

- Samples collected in 2008
- Samples collected in previous years
- Samples collected in 2008 for SVD diagnosis
Regional/National Reference Centres
Reference Laboratories and Collaborating Centres
Additional Reference Centres

Intermediate, sporadic

FMD - Free
Free. Virus present in game parks
Intermediate, sporadic

Pool 1
O, A, Asia 1

Pool 2
O, A, Asia 1

Pool 3
O, A, Asia 1

Pool 4
A, O, SAT 1, 2, 3

Pool 5
O, A, SAT 1, 2

Pool 6
SAT 1, 2, 3

Pool 7
O, A

Source: Annual OIE/FAO FMD Reference Laboratory Network Report, 2007
Multiple origins of a FMD V serotype Asia 1 Epidemic

Memorandum of Understanding

• To encourage sharing of materials and data by providing assurance on wider distribution and disclosure
  – Isolates
  – Reference strains
  – Sequences
  – Vaccine strains
  – Vaccine antisera

• Not all administrations willing to sign
  – Issues remain over who owns viruses and characterisation data and minimum obligations of an OIE RL to release data
Electronic data and communications centre for internal and external use (WRLFMD and FMD Ref Lab Network)

- Laboratory related information exchange between Partners
- Visualisation and interrogation of data
- Merging and harmonising various data sources (internal and external – members’ LIMS, FAO etc.)
- Provision of laboratory based information to FAO/OIE and to the wider scientific community
ReLaIS Intentions and features

• Currently
  – Access to database of information on samples received at WRLFMD including
    • Spatial information
    • Temporal information
    • Species of origin
    • Serotyping
    • Subtyping
    • Vaccine matching data
    • Phylogenies

• Future
  – Automated submission of data by Members
  – Web sample submission and tracking by submitter
Reference Viruses and Sequences

- Currently ad hoc sharing of viruses and sequences between partners
- More generic sharing between partners possible as confidence in system grows?
- ReLaIS can also make sequences available for analysis without release
- WRLFMD initiative to make available viruses and sequences representative of all topotypes with benefits in relation to
  - Test validation
  - Nomenclature harmonisation
  - Molecular epidemiology
  - Framework for vaccine matching
- Guide protocols for VP1 sequencing and analysis
Decision tree for primer* selection for RT-PCR and DNA sequencing

*, Some additional sequencing primers are not shown
Neighbor-joining tree showing the relationship between the VP1 reference sequences representative of all of the main FMDV lineages
<table>
<thead>
<tr>
<th>Topotype</th>
<th>Strain</th>
<th>Isolate name</th>
<th>Accession no.</th>
<th>Reference</th>
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<td>CATHAY</td>
<td>-</td>
<td>O/HKN/21/70</td>
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<td>Knowles et al., 2001</td>
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<td>Knowles et al., 2001</td>
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<td>Beard and Mason, 2000</td>
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<td>EA-1</td>
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<td>O/K83/79* (Kenya)</td>
<td>AJ303511</td>
<td>Samuel and Knowles, 2001</td>
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<td>-</td>
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<td>O/TAN/2/2004</td>
<td>n/a</td>
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<td>Ayelet et al., submitted</td>
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<td>Ayelet et al., submitted</td>
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<td>Carrillo et al., 2005</td>
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<td>Samuel and Knowles, 2001</td>
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<td>-</td>
<td>O/ISA/1/74</td>
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<tr>
<td>ME-SA</td>
<td>-</td>
<td>O/R2/75* (India)</td>
<td>AF204276</td>
<td>Hemadri et al., unpublished</td>
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<tr>
<td>ME-SA</td>
<td>-</td>
<td>O/IND/53/79</td>
<td>AF292107</td>
<td>Hemadri et al., unpublished</td>
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<td>Mason et al., 2003</td>
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<td>O/IRN/8/2005</td>
<td>n/a</td>
<td>Knowles et al., submitted</td>
</tr>
<tr>
<td>SEA</td>
<td>-</td>
<td>O/TAI/189/87*</td>
<td>n/a</td>
<td>From Toru &amp; Wilai</td>
</tr>
<tr>
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<td>Cam-94</td>
<td>O/CAM/3/98</td>
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<td>Knowles et al., 2001</td>
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<tr>
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<td>Mya-98</td>
<td>O/MYA/1/98</td>
<td>AJ303521</td>
<td>Samuel and Knowles, 2001</td>
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</tbody>
</table>
Neighbor-joining tree showing the relationship between the type O VP1 reference sequences

O/UGA/3/2002 (DQ165077)
O/KEN/5/2002 (DQ165073)
O/TAN/2/2004
O/MAL/1/98 (DQ165074)
O/K40/84*
O/K83/79* (AJ303511)
O/UGA/5/96 (AJ296327)
O/SUD/2/86 (DQ165075)
O/ETH/2/2006
O/ETH/3/2004
O/ETH/1/2007
O/ETH/17/98
O/ETH/58/2005
O/GHA/5/93 (AJ303488)
O/CIV/8/99 (AJ303485)
O/TAI/189/87* (TRRL)
O/Mya/7/98 (DQ164925)
O/CAM/3/98 (AJ294910)
O/INd/R2/75* (AF204276)
O/INd/53/79 (AF292107)
O/UKG/35/2001 (AJ539141)
O/IRN/8/2005
O/PHI/7/96 (AJ294926)
O/Yulin/TAW/97 (AF308157)
O/HKN/6/83 (AJ294919)
O/HKN/21/70 (AJ294911)
O/INd/9/74 (AJ303502)
O/INd/8/3 (AJ303503)
O/INd/1/62 (AJ303500)
O/INd/1/74 (AJ303501)
O/JAV/5/72 (AJ303509)
O/Corrientes/ARG/06 (DQ834727)
O2/Brescia/ITL/47 (M55287)
O1/BFS 1860/UK/67 (AY593815)
O3/VEN/51 (AJ004645)
Inter-laboratory Comparison of Antigenic Matching (1)

- How reliable/comparable are vaccine matching data from different RLs?
- Main source of discrepancies likely to be reagents and/or methods
- Pilot trial conducted in 2008
  - To evaluate whether similar results obtained by labs using own methods but harmonised reagents
  - Difficulties overcome over exchange of materials
  - Generated reagents specific for the task
## Virus panels sent to participants

<table>
<thead>
<tr>
<th>Sample</th>
<th>Virus</th>
<th>Virus history</th>
<th>Original “r1” by WRL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A AFG 7/2007</td>
<td>BTY1RS1BHK2</td>
<td>0.33</td>
</tr>
<tr>
<td>2</td>
<td>A EGY 1/2006</td>
<td>BTY1RS1BHK2</td>
<td>0.23</td>
</tr>
<tr>
<td>3</td>
<td>A IRN 5/2006</td>
<td>BTY1RS1BHK2</td>
<td>0.53</td>
</tr>
<tr>
<td>4</td>
<td>A TUR 24/2007</td>
<td>BTY1RS1BHK2</td>
<td>0.81</td>
</tr>
<tr>
<td>5</td>
<td>A IRN 5/2006</td>
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<tr>
<td>Ref. virus</td>
<td>A Iraq 24/64</td>
<td>CP2 BTY2BHK5</td>
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</tr>
</tbody>
</table>
Inter-laboratory Comparison of Antigenic Matching (2)

- Results obtained from 5 RLs for VNT
  - Two labs gave discordant results
- Repeat with more isolates and participants
- Extend to isolates where cross-protection is known
- Try harmonising methodology
- Extend to ELISA as well as VNT
- Extend to additional serotypes
- Bilateral studies also under development
Research to improve vaccine matching

- Cross-protection studies to provide baseline data
- Antigenic cartography to map serological relationships
- Non-neutralising versus neutralising antibodies
- Correlating sequence with antigenic match
Future Considerations

• Maintaining momentum
  – Continued activities and data sharing
  – Enlargement / complementary skills / regional cascade

• Research activities
  – Vaccine matching improvements (FP7 Disconvac)
  – GFRA (Global FMD Research Alliance)

• Political buy-in
  – National support for surveillance and vaccine bank networks
  – International support for coordination activities
  – Securing sustainability (Networking versus twinning)
  – Regional control programmes
Acknowledgement to OIE and FAO and all of the colleagues of the Ref Lab Network in:

- **Pirbright**
- **Rio de Janeiro**
- **Vladimir**
- **Gabarone**
- **Buenos Aires**
- **Onderstepoort**
- **Plum Island**
- **Brussels**
- **Lanzhou**
- **Mukteswar**
- **Pakchong**

**Break-out groups during 2008 Network meeting**

**New vaccine production plant at Lanzhou Campus**
Thank-you for your attention