FMD Trends

Summary
This reporting period has been dominated by outbreaks of FMD in United Kingdom. FMD was initially confirmed on 3rd August 2007 in beef cattle in Normandy, Surrey. Subsequently 8 premises (11 holdings) were found to have animals that were infected by FMDV. These outbreaks occurred in two distinct clusters located around Normandy and Egham in Surrey separated in time by 36 days. Nucleotide sequencing has shown that the FMD virus responsible for these outbreaks is derived from O1/BFS 1680; an isolate used as a reference and vaccine strain at the Institute for Animal Health and Merial Animal Health Ltd located on the Pirbright site. Furthermore, analysis of full-genome sequence data has been used to demonstrate that outbreaks near Egham (IP3-IP8) were derived from infection via the Normandy cluster (IP1 and IP2), and not through a separate escape from the Pirbright site that reintroduced the virus into the field. Investigations have been undertaken to determine the most likely source of these outbreaks; the results from these independent enquiries have been published separately and their findings are available from the following websites:


The following information was collated from OIE (http://www.oie.int/wahid-prod-public.php?page=home), Promed (http://www.promedmail.org/) and the FMD news service at UC Davis (http://fmd.ucdavis.edu/).

Outside of the UK, no outbreaks were officially reported in FMD-free countries that did not practice vaccination between July and September 2007. A new outbreak of type O was reported in European Turkey close to Bulgaria. Cattle in a single village in the district of Kirkcure were infected due to illegal animal movements from Anatolian Turkey. Animals in this region are regularly vaccinated and emergency vaccination was also applied. No subsequent outbreaks have been reported. Elsewhere in the Mediterranean basin, 5 new FMD outbreaks affecting 4 sheep and 1 goat herd in the Palestinian Territory have been reported to the OIE. In common with previous outbreaks in the region, FMDV serotype O has been identified as the causative agent. [UPDATE: Further outbreaks of FMD due to serotype O have been reported recently in Egypt (October 2007) and in Cyprus (late October 2007). Sequence analysis of Egyptian viruses is underway and will be presented in the next report; preliminary analysis indicates that these viruses belong to the new PanAsia lineage that has recently spread through the Middle East. An outbreak of SAT1 occurred in North West Botswana (October 2007) in a region where vaccination is routinely practiced and the outbreak has been attributed to contact with wildlife following flood damage to fencing.]

In early July, China reported a further outbreak of FMD in Qinghai province due to serotype Asia 1. Fifty cattle (yaks) showed clinical signs and the outbreak was controlled by slaughtering 107 cattle and disinfection. In August 2007, FMD outbreaks occurred in Bhutan affecting 5 five ewes of Baro, Goshing, Naigkor, Phangchik and Shangphar in Zhimphang. Material from some of these cases has been received at the WRL and has typed as serotype O (molecular characterisation of these isolates is underway and it is anticipated that this information will be described in the next report). In India, an outbreak of FMD (serotype O) affected a zoo in Tamilnanaannever in July 2007. High mortality in Indian Gaur (Bos Gaurus) and blackbucks was observed. In Vietnam, further FMD outbreaks affecting cattle, buffaloes, pigs and goats have occurred (June-July 2007) in the central province of Quang Tri due to serotype Asia 1. The worst-hit area was Da Krong with over 470 out of 650 animals contracting the disease. In August, FMD spread to Can The city in the Mekong Delta, although the relationship of these outbreaks to earlier cases is not clear. Elsewhere in Southeast Asia, there have also been reports of FMD outbreaks in Myanmar close to Rangoon.

In Africa, the OIE has re-instated FMD free zones, without vaccination to all the zones in Botswana except zone 7 (Bobonong and Selebi-Phikwe area).

In South America, vaccination covering 96% of the local cattle population has been used to control the earlier outbreaks of FMD due to serotype O (in Tiquinquillo, Marabu, Ecuador). In July, there were new reports of an FMD outbreak (due to serotype O) in north-west Venezuela (Zulia), about 60 km from the Colombian border. Furthermore during September 2007, additional cases of FMD were reported in Piar, Bolivar in the east of the country. In central Venezuela, the second round of mass vaccination of 2007 in Zulia will start in October. During the first round 91.5% of the 38,315 cattle in the state were FMD vaccinated. FMD mass vaccination campaigns are continuing in Paraguay, in the Brazilian State of Goias and in the Argentine province of Entre.
The WRL vaccine recommendations remain unchanged although O1 Manisa appears to have only a moderate match against the current O PanAsia strains circulating in the Middle East and a potency test is scheduled to examine the cross-protection afforded in vivo.

Results from samples received to WRL (status of samples being testing is shown in Table 1)

An up-to-date list and reports of FMD viruses characterised by sequencing can be found at the following website: http://www.wrlfmd.org/fmd_genotyping/2007.htm

Europe

FMDV serotype O
VP1 and full-genome sequencing has been performed on viruses recovered from all the infected premises from the FMD outbreak in United Kingdom. These viruses are all closely related to each other and derived from O1 BFS 1860 (see Annex 2, Figure 1).

Africa

FMDV serotype O
Sequencing of an FMDV serotype O isolate from Uganda showed that it was most closely related to other FMD viruses from Uganda (collected in 2004) within the East Africa-2 genotype (see Annex 2, Figure 2).

Middle East

FMDV serotype O
Three FMDV isolates from Yemen have been sequenced belonging to the East-Africa-3 genotype (see Annex 2, Figure 3). 17 serotype O isolates collected during 2007 have also been characterised from Turkey (see Annex 2, Figure 4). This analysis showed that they were all from the new PanAsia lineage widely circulating through the Middle East and South Asia.

FMDV serotype A
Eight serotype A viruses have also been characterised from Turkey (from 2007). All belong to the IRN-05 lineage (see Annex 2, Figure 5).

Table 1: Status of sequencing of samples received recently to WRLFMD

<table>
<thead>
<tr>
<th>Batch</th>
<th>Country</th>
<th>Serotype</th>
<th>No. of samples</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>WRLFMD-2007-00019</td>
<td>Pakistan</td>
<td>O</td>
<td>43</td>
<td>in progress</td>
</tr>
<tr>
<td>WRLFMD-2007-00021</td>
<td>Uganda</td>
<td>O</td>
<td>1</td>
<td>completed</td>
</tr>
<tr>
<td>WRLFMD-2007-00023</td>
<td>Turkey</td>
<td>O</td>
<td>17</td>
<td>completed</td>
</tr>
<tr>
<td>WRLFMD-2007-00022</td>
<td>Turkey</td>
<td>A</td>
<td>8</td>
<td>completed</td>
</tr>
<tr>
<td>WRLFMD-2007-00045</td>
<td>Yemen</td>
<td>O</td>
<td>3</td>
<td>in progress</td>
</tr>
</tbody>
</table>

Vaccine matching

Three isolates (O UKG 7, 9, 11/2007) from 2007 FMD outbreak in UK were antigenically analysed for type O vaccine virus to provide advice on the vaccine selection should the emergency vaccination strategy used. As expected from the sequence data, the results from two dimensional VNT showed that these field strains were closest matched to O BFS, O Campos, O Bansanne and O kauhauen vaccine strains, and also relatively matched to O Manisa vaccine strain (Annex 1, TABLE C).

Twenty one FMDV type O isolates (O ETH 21, 27 and 43/2006, O AFG 29, 34, 36, 37, 39, 42, 43, 45/2007, O PAK 7, 20, 48 and 50/2007 and O TUR 11, 13, 29 and 30/2007) from Ethiopia, Afghanistan, Pakistan and Turkey collected in 2006 and 2007 were further characterised by two dimensional virus neutralisation test (Annex 1; TABLE C), showing that most of these isolates were antigenically matched with O1 Manisa vaccine strain and indicating that the currently predominant type O virus can be covered by a vaccine present in many vaccine banks. Four field isolates received from Vietnam (1, 3, 11 and 12/2007) along with two of above isolates (O PAK 20/2007 and O TUR 13/2007) have showed antigenic matching to O Ind R2/75 vaccine strain.
Nine FMDV type A isolates (A AFG 7 and 44/2007; A Vit 8 and 18/2005; A Esh 6/2006; A Mai 12 and 16/2006 and A Sud 1 and 3/2006) from Afghanistan, Vietnam, Ethiopia, Mali and Sudan have been antigenically analyzed by VNT and LPBE. The results showed that only two isolates from Vietnam provide some match to A22 vaccine strain; the rest failed to match to either A22 or A Ind 17/82 strains. Four isolates from Ethiopia, Mali and Sudan showed antigenic matching to A Eritrea vaccine strain (Annex 1, TABLE C).

Publication of data to the scientific community and the industry

FMD papers published in the reporting period from the Pirbright Laboratory (Pirbright authors underlined):


TABLE B: Summary of samples collected and received to IAH-Pirbright (July – September 2007)

<table>
<thead>
<tr>
<th>Country</th>
<th>No. of samples</th>
<th>Virus isolation in cell culture/ELISA</th>
<th>RT-PCR for FMD (or SVD) virus (where appropriate)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>O A C SAT Atia 1 SVD NVD NT</td>
<td>Positive Negative NT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 2 or 3</td>
<td></td>
</tr>
<tr>
<td>NORTH KOREA</td>
<td>1</td>
<td>- - - 1 - - - - 1 - - - - 1 - - -</td>
<td>- - -</td>
</tr>
<tr>
<td>SUDAN</td>
<td>21</td>
<td>- - - - - - - 21 - -</td>
<td>- - -</td>
</tr>
<tr>
<td>TURKEY</td>
<td>30</td>
<td>17 8 - - - - 5 - - - 29 1 - -</td>
<td>- - -</td>
</tr>
<tr>
<td>UGANDA</td>
<td>31</td>
<td>1 - - - - - 30 - - - 5 26</td>
<td>- - -</td>
</tr>
<tr>
<td>UNITED</td>
<td>2415</td>
<td>95 - - - - - - - - - - - - - - - - 339 1781 98 1798 519</td>
<td>- - -</td>
</tr>
<tr>
<td>KINGDOM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YEMEN</td>
<td>29</td>
<td>3 - - - - - - - 26 - 17 12 -</td>
<td>- - -</td>
</tr>
<tr>
<td>TOTAL</td>
<td>2527</td>
<td>116 8 - - - - - - - - - - - - - - - 621 1781 150 1858 519</td>
<td>- - -</td>
</tr>
</tbody>
</table>

* Institute for Animal Health, Pirbright Laboratory, Woking, Surrey GU24 0NF

V/ELISA FMD (or SVD) virus serotype identified following virus isolation in cell culture and antigen detection ELISA

FMD foot-and-mouth disease

SVD swine vesicular disease

NVD no FMD, SVD or vesicular stomatitis virus detected

NT not tested

RT-PCR reverse transcription polymerase chain reaction for FMD (or SVD) viral genome

** samples from Portugal submitted for SVDV characterisation

NPF, 6 October 2007
TABLE C: Antigenic characterization of FMD field isolates by matching with vaccine strains by ELISA and/or VNT - r Value data from 1st July to 30th September 2007

<table>
<thead>
<tr>
<th>Isolates</th>
<th>( r ) values by 2dmVNT for type O Vaccine strains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>O Maasa</td>
</tr>
<tr>
<td>AFG 29/2007</td>
<td>0.76</td>
</tr>
<tr>
<td>AFG 34/2007</td>
<td>0.46</td>
</tr>
<tr>
<td>AFG 36/2007</td>
<td>0.39</td>
</tr>
<tr>
<td>AFG 37/2007</td>
<td>0.46</td>
</tr>
<tr>
<td>AFG 39/2007</td>
<td>0.38</td>
</tr>
<tr>
<td>AFG 42/2007</td>
<td>0.87</td>
</tr>
<tr>
<td>AFG 43/2007</td>
<td>0.74</td>
</tr>
<tr>
<td>AFG 45/2007</td>
<td>0.85</td>
</tr>
<tr>
<td>PAK 20/2007</td>
<td>0.33</td>
</tr>
<tr>
<td>PAK 48/2007</td>
<td>0.38</td>
</tr>
<tr>
<td>PAK 50/2007</td>
<td>0.56</td>
</tr>
<tr>
<td>PAK 7/2007</td>
<td>0.72</td>
</tr>
<tr>
<td>TUR 11/2007</td>
<td>0.54</td>
</tr>
<tr>
<td>TUR 13/2007</td>
<td>0.50</td>
</tr>
<tr>
<td>TUR 29/2007</td>
<td>0.55</td>
</tr>
<tr>
<td>TUR 30/2007</td>
<td>0.44</td>
</tr>
<tr>
<td>UGA 18/2007</td>
<td>0.5</td>
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<tr>
<td>UKG 11/2007</td>
<td>0.46</td>
</tr>
<tr>
<td>UKG 7/2007</td>
<td>0.69</td>
</tr>
<tr>
<td>UKG 9/2007</td>
<td>0.52</td>
</tr>
<tr>
<td>Vit 3/2005</td>
<td></td>
</tr>
<tr>
<td>Vit 11/2005</td>
<td></td>
</tr>
<tr>
<td>Vit 12/2005</td>
<td></td>
</tr>
<tr>
<td>Vit 1/2006</td>
<td></td>
</tr>
<tr>
<td>Eth 2/2006</td>
<td>0.74</td>
</tr>
<tr>
<td>Eth 21/2006</td>
<td>0.42</td>
</tr>
<tr>
<td>Eth 27/2006</td>
<td>0.36</td>
</tr>
<tr>
<td>Eth 43/2006</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Interpretation of \( r \) values

In the case of VNT:

\( r_1 = \geq 0.3 \)  Suggests that there is a close relationship between field isolate and vaccine strain. A potent vaccine containing the vaccine strain is likely to confer protection.

\( r_1 = < 0.3 \)  Suggests that the field isolate is so different from the vaccine strain that the vaccine is unlikely to protect.
<table>
<thead>
<tr>
<th>Isolates</th>
<th>Test</th>
<th>Vaccine strains</th>
<th>Test</th>
<th>Vaccine strains</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>A22</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ind</td>
<td>17/82</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AFG 44/2007</td>
<td>VNT</td>
<td>0.26</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>AFG 7/2007</td>
<td>VNT</td>
<td>0.29</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Vit 8/2005</td>
<td>VNT</td>
<td>0.33</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>Vit 18/2005</td>
<td>VNT</td>
<td>0.32</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>Eth 6/2006</td>
<td>VNT</td>
<td>0.20</td>
<td>0.46</td>
<td>LPBE</td>
</tr>
<tr>
<td>Mal 12/2006</td>
<td>VNT</td>
<td>0.61</td>
<td>0.43</td>
<td>LPBE</td>
</tr>
<tr>
<td>Mal 16/2006</td>
<td>VNT</td>
<td>0.21</td>
<td>0.21</td>
<td>LPBE</td>
</tr>
<tr>
<td>Sud 1/2006</td>
<td>VNT</td>
<td>0.13</td>
<td>0.33</td>
<td>LPBE</td>
</tr>
<tr>
<td>Sud 3/2006</td>
<td>VNT</td>
<td>0.11</td>
<td>0.34</td>
<td></td>
</tr>
</tbody>
</table>

**Interpretation of r values**

In the case of ELISA,

- $r_1 = 0.4-1.0$. Suggests that there is a close relationship between field isolate and vaccine strain. A potent vaccine containing the vaccine strain is likely to confer protection.
- $r_1 = 0.2-0.39$. Suggests that the field isolate is antigenically related to the vaccine strain. The vaccine strain might be suitable for use if no closer match can be found provided that a potent vaccine is used and animals are preferably immunized more than once.
- $r_1 < 0.2$. Suggests that the field isolate is so different from the vaccine strain that the vaccine is unlikely to protect.
Annex 2: Phylogenetic analysis of characterised FMDV isolates:

Fig 1 Molecular characterisation (based on VP1 sequence) of serotype O FMDV causing outbreaks in the United Kingdom.
Fig 2 Serotype O from Uganda


Software: MEGA 3.1
No. of Trees: 127
Data File: MobilinjugbfohnoWUOG2007a.meg
Data Type: Nucleotide (Coding)
Analysis: Phylogenetic reconstruction

Trees Inferred: 

Method: Neighbor-Joining
Phylogeny Tree and colors: Bootstrap (1000 replicates; seed=64238)
Induced Sites: 

Data/Viewing Data: Fanwise Detection
Color Positions: 1st-2nd-3rd-Noncoding

Substitution Model: 

Model: Nucleotide, Kimura 2-parameter
Substitutions to include: 9 Transitions + Transversions
Pattern among Lineages: Speciation (Homogeneous)
Rates among sites: Uniform rates
No. of sites: 542
No of Bootstrap Maps: * 1000
Only bootstrap values of 70% and above are shown
*, not a WHO/FMD Ref. No.

N.J. Knowles & J. Wadsworth, 9 August 2007
Fig 3 Serotype O from Yemen

Report on FMDV O/Yemen/2006

Software: MEGA 3.1
No. of taxa: 130
Data File: -nfile=MEGA/MEGA06a.tree
Data Title: O Yemen 2006
Data Type: Nucleotide (Coding)
Analysis: Phylogeny reconstruction
Tree inference: -------------------------------
Method: Neighbor-Joining
Phylogeny Test and options: Bootstrap (1000 replicates: seed=62346)
Include Sites: ---------------------------------
Gap/missing data: PAUP* default
Color Positions: 1st+2nd+3rd+Noncoding
Substitution Model: -------------------------------
Model: Nucleotide: Kimura 2-parameter
Substitution tests: include: d: Transitions + Transversions
Rate among lineages: Same (homogeneous)
Rates among sites: Uniform rates
No. of Sites: 642
No. of Bootstrap Reps = 1000
Only bootstrap values of 70% and above are shown.

N.J. Knowles & J. Wadsorth, 15/01/2007
Fig 4 Serotype O from Turkey

Report on 17 FMD type O viruses from Turkey in 2007

Software: MEGA 3.1
No. of Trees: 107
Data File: m4level1magd1/4/4/4/TUR2007b.m4g
Data Title: O Turkey 2007
Data Type: Nucleotide (Coding)
Analysis: Phylogeny reconstruction
Tree Inference: 
Method: Neighbour-Joining
Phylogeny Test and options: Bootstrap (1000 replicates; seed=04230)
Include Sites: 
Gaps/Missing Data: Nucleotide Deletion
Codon Positions: 1st+2nd+3rd+Noncoding
Substitution Model: 
Model: Nucleotide Kimura 2-parameter
Substitutions to Include: d: Transitions + Transversions
Pattern among Lineages: Same (Homogeneous)
Rates among sites: Uniform rates
No. of Sites: 330
No. Of Bootstrap Reps = 1000
Only bootstrap values of 70% and above are shown

N.J. Knowles & J. Wadsworth, 12 September 2007
Fig 3 Serotype A from Turkey

Report on 8 FMD type A viruses from Turkey in 2007

Software: MEGA 3.1
No. of Taxa: 133
Data File: n:evd/seq/db/fmdv/VarTUR2007b.maf
Data Type: A Turkey 2007
Data Type: Nucleotide (Coding)
Analysis: Phylogeny reconstruction
Tree Inference: =============================
Method: Neighbor-Joining
Phylogeny Test and options: Bootstrap (1000 replicates; see p.228)
Include Sites: ===============================
Gaps/Missing Data: Pairwise Deletion
Codon Positions: 1st+2nd+3rd=Noncoding
Substitution Model: ===============================
Model: Nucleotide: Kimura 2-parameter
Substitutions to Include: d: Transitions + Transversions
Rate among Sites: Uniform rates
No. of Sites: 640
No Of Bootstrap Reps = 1000
Only bootstrap values of 76% and above are shown

N.J. Knowles & J. Wadsworth, 12 September 2007