EURL for foot-and-mouth disease
Examples of coordination, advice, training and surveillance activities

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Impact of FMD

The cull widens as the contagion grows

DEADLY VIRUS THAT HAS SHUT DOWN THE COUNTRYSIDE

Foot-and-mouth crisis: The tragedy unfolds
The Pirbright Institute
Our science

Research at the Institute is a synergistic combination of fundamental and applied science, based upon a wide range of expertise, and unique biological and physical resources. The science strategy is delivered through three strategic programmes:

- **Avian Viral Diseases**
- **Livestock Viral Diseases**
- **Vector-borne Viral Diseases**

Each programme comprises a platform of fundamental science projects that provide the new knowledge that is then translated, within the programmes, into applied science.
BBSRC National Virology Centre: The Plowright Building

- 2015: Occupied new high containment laboratory
- Houses all our work with “live” FMD and International Reference Laboratories for FMD, BT, PPR, ASF, AHS, Capripox
New low-containment building

- Containment Level 2 Laboratory
- Work started in 2013
- Commissioned 2015-16
- Cost £15m
National Reference Laboratory (NRL) for FMD

Core activities:

• Diagnostic service (24/7) for suspect national REPORT cases providing *timely* and *reliable* results
• Ability to respond in the event of an FMD outbreak in the UK
• Contingency planning (in the event of a future FMD outbreak)
• Development and validation of improved tests and vaccines
• Advice to UK Government regarding vaccine selection, control policies and global threats
FMD: Conjectured global status

- Seven FMDV serotypes
- Seven endemic pools requiring tailored diagnostics and vaccines
- Europe is FMD-free (without vaccination)

• Threats from outside Europe!
EU Reference Laboratory for FMD
• Support improvements in diagnostic performance of NRLs for EU member states
• Provides assistance and referral diagnostic capacity for EU member states

OIE Reference Laboratory
World Reference Laboratory for FMD
• To safeguard international trade
• To support global initiatives for FMD control
• Characterisation of field outbreaks
• Supply of reagents
• Maintain contact with other OIE and FAO laboratories
• Provide advice regarding appropriate tests for inclusion in the *OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*
EU Reference Laboratory for FMD

- Surveillance
- NRL Performance (PTS)
- Training
- Research opportunities
Viruses on the move:
Changing epidemiological patterns (2013-16)

Outbreaks reported to the OIE (change of epidemiological status):
Recent serotype O cases

- O/ME-SA/Ind2001 lineage from the Indian sub-continent
- Since 2013: FMD Outbreaks in Saudi Arabia, UAE, Bahrain, Libya, Tunisia, Algeria
- Transmission links unknown?

Knowles et al., (2015) TED
Increased threats of FMD to Europe?
Preparing for an outbreak: Vaccine Potency Trial

- Funded via EU (from EU-RL) contribution
- Experiments hosted by CVI-Lelystad (The Netherlands)
- Field virus provided by IZSLER-Brescia (Italy)
- Adopted protocol according to European Pharmacopeia
- O-Manisa vaccination (at least $6\text{PD}_{50}$) with O/ALG/2014 challenge

<table>
<thead>
<tr>
<th>Vaccine Dose</th>
<th>Number Protected vs Vaccinated</th>
<th>Serological Results (O Manisa $\log_{10}$ VNT mean 21DPV)</th>
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<tbody>
<tr>
<td>Full</td>
<td>3/5</td>
<td>2.65</td>
</tr>
<tr>
<td>1/4</td>
<td>4/5</td>
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<tr>
<td>1/16</td>
<td>0/5</td>
<td>1.68</td>
</tr>
<tr>
<td>Unvaccinated*</td>
<td>0/2</td>
<td>0.9</td>
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</tbody>
</table>

- Results fed back to EU NRLs
Impact of surveillance

- Recognition of new and emerging viral lineages
- Patterns of virus movement
- Understanding threats
- Early warning and contingency planning
- Performance of vaccines
  - Advice to EU-vaccine bank managers at DG-SANTE
- Validation and improvement to diagnostic tests

NRLs play an important role as the “eyes and ears”
- Bulgaria 2010-11

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NRL capability (EU member states)

• Agreed minimum capabilities for a NRL:
  1. laboratories should be able to detect FMDV virus in clinical specimens
  2. laboratories should be to correctly identify animals previously exposed to FMDV by serology

• Particular tests and assays are not specified: laboratories must select appropriate tests, and use them to interpret the status of the samples
Broads aims of the proficiency testing scheme:

- Intra-laboratory equivalence testing
- NRLs from all EU member states must participate or delegate responsibility to another NRL
- To assist NRLs to employ accurate and reproducible FMD diagnostic tests
- Feedback (reiterative improvements to assays)
- Quality assurance programme requirements to support ISO/IEC 17025
- Covers SVDV* as well as FMDV

*From Jan 2015 the EU will not support an EU-RL for SVDV
History of past intra-laboratory comparative exercises for FMD

• 1977: Results from Phase I reported at Brescia
  – 21 laboratories participated
  – Compared VI and VNT methods
  – Reported difficulties in logistics and in sample shipment

• 2005: Pilot study involving 5 labs to test feasibility of including virus detection assays (VI and RT-PCR)

• 2005-6: Phase XIX first exercise to include molecular assays for virus detection

• 2014: Phase XXVII reported and completed

• 2015: Phase XXVIII initiated
Challenges in preparation of the PT panels

- Multiple FMDV serotypes complicates ability to detect virus or antibody

- FMDV detection (VI, RT-PCR and ELISA):
  - Which isolates/serotypes are represented?
  - Contemporary strains
  - Relevant biological matrix – ideally field samples

- Serology (SP and NSP)
  - Host species and serotype of virus
  - Purpose in relation to vaccination: DIVA, vaccine coverage
  - Accommodate different assay formats with differing se/sp
  - Individual vs herd-based (different purpose and cut-off)

- Large amounts of material are required!
EU Phase XXVII Participants:

- Infectious **Panel 1** only sent to 12 labs (2014/15 reports)
- All labs receive non-infectious material and serology panels

- PT panels also sent to EU neighborhood countries:
  - Switzerland, Norway, Turkey, Serbia, Bosnia and Herzogovina, Belarus, Albania, Macedonia etc.....

<table>
<thead>
<tr>
<th>Country</th>
<th>Panels</th>
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<tr>
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<tr>
<td>Austria</td>
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<td>Belgium</td>
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<tr>
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<td>Denmark</td>
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<tr>
<td>Estonia</td>
<td>x</td>
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<td>Finland</td>
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<td>France</td>
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<td>Germany</td>
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<td>Greece</td>
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<td>Sweden</td>
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<tr>
<td>United Kingdom</td>
<td>✔</td>
</tr>
</tbody>
</table>

**Total** (labs/countries): 12 26 26 26
Bench-marking of results

- Independent 10x testing is undertaken at Pirbright to demonstrate the robustness of materials in the different panels
- Individual results reported with respect to these 10x results
Scoring criteria for NRL performance

- Overall scoring criteria (agreed by the NRLs in 2014):
  - **(Category 1)** to emphasize critical issues where immediate action is required that impact upon the laboratory to correctly identify FMD virus (virology tests) or FMDV infected animals (serological tests)
  - **(Category 2)** laboratories with serious issues with the performance of individual tests that need to be addressed
  - **(Category 3)** to record additional observations which may need to be considered by the laboratory to improve the local performance of individual tests
  - **(Category 4)** laboratories whose tests which are fit for purpose and where no further action is required
Overall performance of EU NRLs

- Data for Phase XXVI (reported in 2014)
- 26 EU NRLs
- Data combined for assays across all the panels (where appropriate)
- Overall performance is improving
Reporting of Results:

- NRL (and other participating labs) report results to EU-RL
- Results confirmed by email with NRL
- Results decoded and fed back to labs
- Interpretation of results and advice to labs
- Reporting of data to scientific community (laboratory identities kept anonymous)
- **Annual Workshop (meeting) of EU NRLs**
- Summary of results reported to EU and EUFMD
Annual EU NRL Workshop
Networking opportunities!
Training activities

Annual training course on FMD diagnostics

FMD diagnostics training course – April 2013

New rapid diagnostics – May 2014

Vaccine matching training course – Sept 2013

Tanzania 2014

Tanzania 2014

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Rapidia-field project

- Evaluation of field and rapid diagnostic tools for veterinary diseases
- Links with industry – routes to commercialisation
- Partners in UK, Spain, Germany, France, Belgium, Switzerland and Sweden
EpiSeq project

Epi-Seq aims to exploit NGS technologies to:
• Generate improved tools for use in real-time monitoring of epidemics
• Collaborators: Belgium, Germany, UK, Italy and Sweden (and Denmark)

Target important RNA/DNA viruses:
• Causing epidemic disease (FMDV/AIV)
• Causing endemic disease (CSFV)
• 2 DNA viruses (ASFV and Poxviruses)

Results will bring novel insights into:
• Field epidemiology: monitor trans-boundary movements
• Evolutionary ecology: genetic determinants underpinning phenotypic traits
Summary, priorities and opportunities:

• Global situation relating to FMD is very dynamic and there are increased threats to Europe (and the neighborhood)
• The NRL Network is critical for the early recognition of FMD virus incursion into the FMD-free countries of Europe
• The PT ensures that basic diagnostic competence is maintained across the network
• **Open and transparent sharing of information is vital**
• Links to other international networks of the OIE and FAO
• Synergies within the network of EU NRLs can be used to efficiently address specific gaps
• Also... there are benefits from national collaborative research initiatives across disciplines (animal, plant and human health)

• Financial support for EU-RL and NRL capacity is declining and needs to be more secure
Acknowledgements

• Funding from the EU for the EU-RL for FMD
• UK - Defra
• Funding from EuFMD (via EU) for support for the PT
• Collaborating FMD Reference Laboratories and field teams
• Partners within the OIE/FAO FMD Lab Network