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

OIE/FAO FMD Reference Laboratories Network Meeting
Lanzhou, China, 15 – 19 September 2008

Participants

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

David Paton John Bashiruddin (Rapporteur) Yanmin Li	OIE Reference Laboratory and FAO World Reference Laboratory for FMD, IAH-Pirbright, UK
Gaolatlhe Thobokwe Elliot Fana Keabetswe Maogabo	OIE FMD Regional Reference Laboratory for the Sub-Saharan continent, Botswana
Vladimir Borisov Alexey Scherbakov	OIE Regional Reference Laboratory for FMD for Eastern Europe, Central Asia and Transcaucasia, FGI-ARRIAH, Russia
Ingrid Bergmann	FAO/OIE Reference Laboratory for FMD, Centro Panamericano de Fiebre Aftosa OPS/OMS, Rio de Janeiro, Brasil
Eduardo Maradei	OIE Reference Laboratory for Foot and Mouth Disease, Laboratorio de Fiebre Aftosa de la Dirección de Laboratorios y Control Técnico, Argentin
Belinda Blignaut	FAO/OIE FMD Reference Laboratory, transboundary Animal Diseases Programme, ARC-Onderstepoort Veterinary Institute, South Africa
Samia Metwally	FAO FMD Reference Laboratory, Foreign Animal Disease Diagnostic Lab, Plum Island Animal Disease Center, Greenport, USA
Kris De Clercq Nesya Goris	OIE collaborating centre for validation, quality assessment and quality control of diagnostic assays and vaccine testing for vesicular diseases in Europe, CODA-CERVA-VAR, Ukkel, Belgium
Xuepeng Cai, Youngguang Zhang, Xiangtao Liu, Hong Yin, Zaixin Liu, Zengjun Lu etc. (see Annex F)	National FMD Laboratory, Lanzhou Veterinary Research Institute, CAAS, Gansu, P. R. China
Divakar Hemadri	Project Directorate on FMD, Indian Council for Agricultural Research, Mukteswar, Nainital (Uttarakhand), India
Wilai Linchongsubongkoch	Regional Reference Laboratory for Foot and Mouth Disease in the South East (RRL), Department of Livestock Development, Pakchong, Thailand
Keith Sumption	EUFMD, Animal Health Division, FAO, Rome, Italy
Kenichi Sakamoto (SCAD)	National Institute for Animal Health, Ibaraki, Japan
Fusheng Guo	FAO Beijing Office, Beijing China

Dr Gideon Bruckner was invited and apologies for his absence were received.

Conclusions

1. Reaffirmed network emphasis
   a. Two principal goals
      i. Global virus distribution and vaccine recommendations
      ii. Improving the quality of laboratory tests for international and national reference laboratories
   b. The Network Partnership also offers opportunity to cooperate in development and validation of diagnostic tests but this has a lower priority

2. Harmonisation of vaccine matching is the current priority for inter-laboratory comparative work between partners

3. The Network may be further expanded by accession of additional FAO Reference Centres

4. The Network's Reference Laboratory Information Centre (ReLaIS) is now live and will be used to improve data sharing, collation and display

5. The Network's Annual Report and the Vaccine Recommendations will be presented on a Regional basis with boundaries defined by natural virus ecosystems

6. A strategy will be developed for the Network to enhance quality of test provision by

Actions Arising

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

1. Vaccine matching inter-laboratory comparison follow-up
   a. Partners to complete first round of testing including LPBE
   b. Secretariat to distribute template to get details of methodology used by participants
   c. Secretariat to request information on reagents remaining with participants
   d. Secretariat to propose a SOP to fully describe methodology for eventual inclusion in OIE manual
   e. Secretariat to circulate a plan for next round of testing incorporating
      i. Analysis of methods used and proposal for standardised approach
      ii. Repeat of initial tests with/without standardised methodology including possible supply of cell lines and additional reagents
      iii. Circulate additional A isolates for matching based on those for which cross-protection to A22 established
   f. Secretariat and partners to develop a plan for type O future work including a schedule for preparation of additional reagents and a costing
   g. Secretariat and partners to develop an outline of research needs in support of vaccine matching
   h. Partners to prepare plans for bilateral or trilateral studies, e.g. on SAT strains for African labs and WRL
      i. An inventory of viruses and sera available at laboratories should be made available
2. Next meeting
   a. Secretariat to liaise with Divakar Hemadri to ensure that arrangements for next meeting in India are feasible.
3. Annual report
   a. Secretariat to compose and circulate proposal for headline summary, regional vaccine recommendations and a template for partners to submit characterisation data to ReLaIS
   b. Use “virus pool” format for subsections
   c. Arrange teleconference in early January to agree steps for finalisation of report
   d. Partners to submit all inputs by January 19th 2009, so that Secretariat can finalise report by end of January
   e. FAO to investigate publishing the Report (as a joint FAO/OIE publication), with additional epidemiological analyses section added by FAO and possibly OIE.
4. Secretariat to re-register participants to ReLaIS
5. Secretariat to prepare draft minutes and actions in time for SCAD meeting at end of September

6. Network to develop a strategy for enhancing quality accreditation of international and national reference labs (Kris De Clercq to lead).
   a. Encourage establishment of regional PTS and encourage the inclusion of internationally recognised advisory boards
   b. Consider ways to provide statistical supportc. Develop guidelines for batch control of commercial tests
7. Consider ways of overcoming communication gaps at Network Meetings
   a. Need more detailed preparation of agenda and circulation of objectives and draft documents prior to meetings so that participants better briefed
8. Nomenclature of FMD viruses
   a. Review plan for naming of isolates
   b. Arrange meeting between WRLFMD and OVI to discuss system for naming of strains, vaccine strains and topotypes for consideration by other partners
9. Exchange of viruses
   a. S. Metwally to re-examine MOU and consider alternative ways to encourage exchanges
   b. Revisit idea of reference/representative strains that could be shared (e.g. panel for which WRL has provided VP1 sequences?)

Day 1

1. Introduction

Hong Yin (HY) welcomed the participants to Lanzhou, China and invited Prof Xuepeng Cai, Director of Lanzhou Veterinary Research Institute (LVRI) to initiate the official opening of the meeting.

Mr. Liang Jiang (LJ), Director of the Veterinary Bureau, Gansu Province, China, welcomed all participants to the province. He explained that livestock industry and animal husbandry were important to the region. Veterinary training was provided within the region and the LVRI was an important addition and resource for Gansu. He stressed the global significance of FMD and therefore the importance of scientific collaboration with China and the world on FMD.

Prof. Xuepeng Cai (XC) welcomed all to the Network meeting and thanked David Paton, John Bashiruddin and Yanmin Li for their help and support. XC presented a brief history of the LVRI from its beginnings in 1957 affiliated to the Chinese Academy of Agricultural Science, Ministry of Agriculture of China. Its sphere of activity included bacteria, parasite and virus infections of livestock and concerning the later FMD, SVD, CSF, PPRS, PCV, sheep pox and PPR are studied here. FMD was an important part of the long history of the LVRI and the reference laboratory was established here in 2003. Today, 16 senior scientists, 77 junior scientists and 40 support staff headed by Dr. Xiangtao Liu work in it and study epidemiology, immunology and biology of FMD/SVD and provide technical services nationally and to provincial laboratories. Research at LVRI provides support for government in the control of FMD and to date we have developed 6 diagnostic tests and 4 quantitative tests for FMD. Vaccines are also produced here and the laboratory plays a crucial role in the quality control. Prof. XC also introduced the participants to the city of Lanzhou and wished them a pleasant stay.

It was an honour to hear from Mr. Jinxiang Li, Director General, Veterinary Bureau, Ministry of Agriculture, China, who congratulated the Network and welcomed meeting participants. China has a very large animal industry e.g. 1st in the world for egg production, 3rd in the world for milk production; it produces 50% of the world's poultry and pigs and, in this setting, the control of animal diseases is very important to the government. Through improvements in veterinary structure and control (immunization and stamping out) huge progress has been made to reducing animal diseases. Globalization means that there are no boundaries to the spread of animal diseases such as FMD and AI and these pose threats to animal and human health. Our aim is to control and eradicate these diseases. LVRI as the national reference laboratory for FMD has achieved good infrastructure (biosecurity laboratory), training and research and is collaborating with the WRL. This Network Meeting in Lanzhou is beneficial to China who wish to work together in information exchange and to LVRI who will play a significant role in global eradication of FMD. I wish you success for this meeting and thank you.

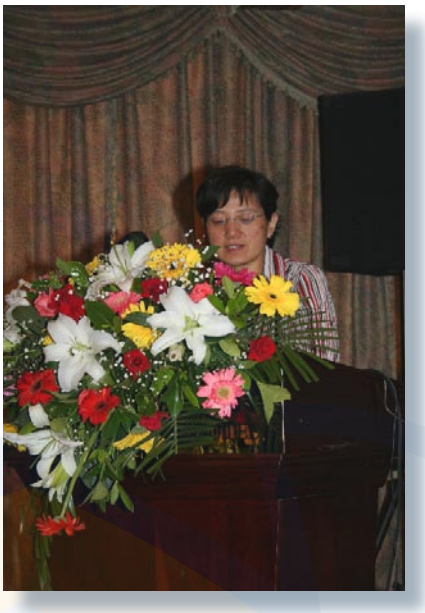
David Paton (DP) welcomed all participants and thanked Mr. Jinxiang Li, Mr. Liang Jiang, Prof. Xuepeng Cai and Dr. Hong Yin for their generosity and warm welcome to China.

Xiangtao Liu thanked DP and participants and gave an overview of the reference activities of the FMD laboratory. Major activities were production of diagnostic reagents, technical services, virus bank, and consultation to the government, international cooperation and communication. Major roles were FMD prevention, diagnosis and vaccines. Major research areas were inactivated vaccines, new types of vaccines, diagnostic methods – serology and antigen detection, molecular evolution, mechanisms of infection and pathogenicity and risk analysis.

Zengjun Lu provided an overview of FMD research at the LVRI. Studies included the development of a reverse genetics system in which virus could be rescued from permissive cells out of full length DNA clones. Using this system VP1, 3A and 5'UTR genomic regions were identified as virulence mechanisms. Mutations in RGD to RDD induced increase in plaque size. Cell lines expressing FMD receptor genes of cattle and Bactrian camels were established. Development of conventional and molecular vaccines was ongoing including adenovirus recombinant but immunity to the vector was a problem with the later. Multiple epitope vaccines, edible vaccines and DNA vaccines were also studied. Diagnostic techniques for virus isolation, penside lateral flow/strip devices, virus typing RT-PCR, universal multi RT-PCR, real time RT-PCR, LPBE and various other ELISA tests were under development or being used.

Eduardo Maradei (EM), from SENSA, the newly appointed OIE Reference Laboratory in South America, gave an overview of the FMD situation in Argentina. The distribution of susceptible animals, the eradication programme and OIE status of zones within the country, systematic vaccination with trivalent vaccine were explained. Following a 2 step random selection of cattle, serological surveys using 3ABC ELISA confirmed with western blots on positives are used to assess infection. Positive cattle were re-sampled for serology and probing samples were taken. Sheep are not vaccinated in Argentina and LPBE is used for their assessments. All the cattle in the northern buffer zone are tested and there is adequate immunity and no virus circulation. Animal movement is controlled via an animal transit document that covers transit waybill and a certificate of animal washing. Subregional projects were mentioned. Activities in modern, well equipped laboratory included diagnoses with a range of current serological and molecular tests, vaccine matching, vaccine QC, reagent production, research in collaboration with INTA and CEVAN and Biogenesis Bago S.A. and biosafety.

2. Vaccine matching trial and vaccine recommendations



David Paton (DP) introduced the OIE/FAO FMD Reference Laboratories Network (Network) to all participants especially the two newly appointed reference laboratories, CODA and SENASA. Collecting outbreak and surveillance information and exchanging information were key objectives of the Network. DP expressed his wish for the network that started in 2004/5 to work more closely together. Keith Sumption added that as more Reference Centres would inevitably be approved there was a greater need for all Network members to contribute actively to plan the work.

Yanmin Li (YL) reminded participants of the aims and expectations of the collaborative trial on vaccine matching planned and agreed in the previous Network meeting. The choice of a prototype vaccine and field isolates used for the exercise and experimental processes of producing vaccine (A22), 5 bovine vaccine serum (bvs), guinea pig and rabbit antiserum produced by OVI and other reagents were explained briefly. Participants in the trial were IAH, RRLSSA, OVI, ARRIAH, FADDL, RRLSEA, LVRI, PDFMD, (PANAFTOSA was invited, but no inactivated reagents were sent to perform the trial) and encrypted samples were sent to all. Collated results were presented and discussed. It was apparent that not all labs obtained similar results despite using the same vaccine virus, bvs and field isolates and that the results of two labs were particularly discordant. Some differences in r-values were obtained for bvs from different cattle. Differences in methodology might explain the variation between labs. There did appear to be good repeatability within labs and pooling of bvs gave similar results to averaging results from individual sera.

In discussions it was surmised that at least 5 sera may be necessary for a pooled sample, which could then be used as representative of one sample in the VNT to generate r1-values. The use of more animals to generate sera was suggested, but this would be a costly exercise. The cut-off values used differed between laboratories; where most laboratories used values of < 0.3 and ≥ 0.3, BVI and OVI used values of 0-0.19, 0.2-0.39 and ≥ 0.4 for the SAT types in Southern Africa. The interpretation of r1-values was discussed and it was emphasized that these values should be interpreted with caution. Multiple field isolates should be used to accurately determine r1-values, as there may be variations within an outbreak. The methodology/rationale used concerning repeats of tests was questioned. Some laboratories repeat the test if dissimilar results are obtained for two repeats of the same sample. Some laboratories routinely use pooled sera.

Several options for further actions were proposed: it was agreed that all partners should complete the first round of testing including LPBE where appropriate; details of methodologies used needed to be gathered; if sufficient reagents remained with participants then testing should be repeated perhaps using a unified methodology; and more isolates of type A could be circulated. PANAFTOSA reiterated its interest in participating in this extended exercise, particularly with LPBE with inactivated samples. The names of the FMD strains used in vaccine and bvs production should now be made available to the trial participants. It was also suggested that the raw data is made available (individual r1-values) for each laboratory to conduct their own comparisons. It was recognized that regular meetings on vaccine matching should be organized and laboratories should participate in a continuous manner in the collection of information regarding new strains emerging in the field.

In the meantime, plans would be developed to do similar work with type O isolates. It was envisaged that eventually standardised methods could be revised/ developed for inclusion into the OIE Manual. The need for further research work on vaccine matching was highlighted and members were encouraged to work together on types and strains that were important in their region. (IB noted that it is difficult to imagine a unique standardized method for the OIE manual before further research provides satisfactory results.)

Day 2

Yongguang Zhang presented a new method for vaccine potency testing in pigs that used challenge virus prepared by passaging in suckling mice rather than in cell cultures, in order to maintain virulence. A modified PD50 test is now used in which three groups of five pigs receive full, one third and one ninth volume doses of vaccine and a fourth control group of two pigs is unvaccinated. The challenge virus is titrated in pigs before administration at 1000 ID50 by the intramuscular route. To date, ~90% of 200 batches tested have passed at the 3 PD50 cut-off.

Keith Sumption added his welcome to all the participants. FAO and OIE, in a series of meetings have discussed strategy, understanding and long term prospects for global FMD control. It is recognised that the Network is a very important part of the strategy because it is a major surveillance structure. Furthermore, the epidemiology of FMD has a regional variation that is reflected in the range of topotypes present in any given region. Therefore, the borders of regions can be seen as 'watersheds' for topotypes. Regions divided by watersheds were not political structures but straddled or divided countries. The concept of watersheds formed the basis for further discussions on vaccines and surveillance. Main areas of endemic foci were depicted as 7 'pools' of topotypes. These areas were corrected slightly by participants and a map is provided in Annex A. The main question was - could vaccine strains tailored to cover the needs of particular regions be identified and provide better, more targeted, regionalised vaccine recommendations?

Four discussion, groups were organised that reflected virus pools or collection of pools as follows: Group 1 – Pool 1; Group 2 – Pool 2 and 3; Group 3 – Pool 4, 5, 6; and Group 4 – Pool 7 (see Annex A). Groups were asked to assess the position of watersheds, list the vaccine seed viruses appropriate for each ecosystem and its priority in 2008 and to consider what additional work is needed to improve these priorities and for better FMD control. A summary of the discussions is provided in Annex B.

3. Global Surveillance, Information exchange and Reporting

David Paton gave a presentation on behalf of Nick Knowles, summarising what is known about the different topotypes found worldwide and latest efforts by WRLFMD to provide a list of representatives of each. Via ReLaIS, it is now possible to obtain this list and the associated VP1 sequences which should be of great value for phylogenetic characterisation of new isolates. It would also make sense to develop a list of vaccine strains known to provide some level of protection for each topotype. A further goal is to agree on the definition of the terms topotype, strain and isolate and to seek a consensus on the nomenclature for each. There followed a discussion, chiefly on the nomenclature of isolates. There was a consensus on the need to include the serotype and year and that the designation should be globally unique. The format Serotype/country/laboratory/sample number/year of isolation e.g. O/TUR/IAH/1/2010 addressed most needs, using a 3 letter country code and a 3 letter laboratory code, and where the sample number reflected individual samples in a batch and a 4 number year was used. Some participants also favoured inclusion of a regional designation, e.g. county/state. IB raised the need to include county and week of isolation to avoid identical naming for different viruses, particularly as occurs in endemic situations. A small group should consider this further in conjunction with Nick Knowles.

John Bashiruddin gave an overview of the ReLaIS website including the mapping facility and reminded members that registration was necessary for access to the private members area of www.foot-and-mouth.org. The phylogenetic analysis module was complete but access was pending suggestions and provision of the list of prototype viruses by WRL. A list was recently available on the WRL website and comments from Network members on the validity of this list would be most welcome.

Samia Metwally informed the meeting of the newly formed North American National Animal Health Laboratory Network. She outlined their activities in 2007 relating to the harmonisation of diagnostic tests which had involved the creation and circulation of may sample panels. The laboratories would continue to work towards regional harmonisation of diagnostic tests and proficiency testing.

Keith Sumption explained the difficulties and expense of shipment of samples to reference laboratories. He asked participants if inactivated samples of serum, nucleic acid from tissue samples or material collected on lateral flow devices were adequate for surveillance purposes. A new, simple and more rapid transport method would increase coverage and surveillance activities that would lead to faster control decisions.

To look at Surveillance Priorities, participants assembled into their previous regional groups and considered problems affecting decisions on vaccine by region, what to do (cost effective actions) and where the surveillance effort should be focused. A summary of discussions is provided in Annex C.

David Paton revisited the format and content of the Network report. There was a pressing need for all members to contribute to the report and to ensure its timely completion. Plans were made to gather relevant information by mid January 2009. It was agreed that the general style of the report should remain essentially as in previous reports but that regional overviews should follow the virus ecosystem boundaries/pools as described early in Day 2. The report should be written in 2 parts; Part 1 – Global virus distribution and characterization, and Part 2 – Network activities on harmonization and the title of the report should be changed to reflect the two parts of the report. It was agreed in principle that virus characterization information could be made available in near real time to OIE and FAO and for collation into the report through ReLaIS, and members agreed to enter this information on line.

KS suggested that the Network Report is submitted as per current practise to both OIE and FAO as soon as possible in early 2009, then with an additional FAO (and perhaps OIE) section, published and printed by FAO. This would raise visibility and create output reflecting the excellent work of the network.

Preliminary information on out-breaks and situations in 2008 for inclusion in the Network Report are summarized in Annex D.

Day 3

4. External QA

Kris De Clercq (KDC) presented some background on external quality assurance programmes and focused on the importance for proficiency testing (PT) for performance evaluation of National Reference Laboratories (NRLs) and Regional Reference Laboratories (RRLs), the production and validation of Reference Standards and the need for international validation and certification of diagnostic assays.

PT is an essential element of accreditation and it became clear that PT would help laboratories towards accreditation as it provides solid external evidence for accreditation authorities that work was within Quality frameworks. He explained the need for appropriate defining the scope of the PT, use of statistics, the criteria for PT, reporting, choice of samples and reference materials, and that these should be agreed at the beginning of the programme. There should be a structure to manage the programme that includes lead laboratories, advisory board and a mechanism for follow up such as feedback from participants and corrective actions by the participants. It was recognised that qualitative assessments could be made first given the difficulties in performing quantitative assessments of laboratories. The organisation of PT and the production of International Reference Standards represent a considerable workload and adequate financial resources are urgently needed.

He stressed that PT would be a natural and worthwhile progression from the collaborative trials already undertaken by the Network. PT could be harmonised by the network. Therefore, decisions on the choice of samples, tests to be included etc. needed to be considered. In fact, the EU Community Reference Laboratory (CRL) conducts a PT programme for the EU National Reference Laboratories (NRL) and participation in this scheme would be appropriate for the Network. The most appropriate scheme – small panels more frequently or comprehensive panels less frequently was discussed. Indeed, some network participants were part of regional PT.

Batch control of kits was discussed and it was apparent that not all manufacturers provided this facility and that a Reference Laboratory may need to do this. Going around the table amongst participants, it was evident that some of the laboratories were taking a lead on regional PTS and others were not yet doing so and that there is therefore scope for the participants to share best practice and assist one another in the provision of reagents and development of advisory boards. KDC agreed to liaise with WRL and OVI to prepare more concrete suggestions for the way forward.

5. Future Directions and Developments

Keith Sumption informed the meeting about the EUFMD Open Session in Erice, Sicily (Italy) 14-17 October 2008, where several participants were giving keynote presentations. There is a scheduled time for David Paton to report on Network activities in this meeting.

The upcoming OIE pledging meeting June 26, 2009, in Asunción, Paraguay was mentioned where the FAO/OIE global approach to FMD control and eradication will be considered and where it is expected that the Network will be able to contribute significantly.

John Bashiruddin informed the meeting of the submitted COST project of 5 years duration that if successful would provide financial assistance for future Network meetings.

Networking and its relationship to the OIE twinning concept were discussed. There may be scope for exploring with OIE how twinning may be applied to Network support.

Network priorities (over the next 5 years) were discussed in groups and are in Annex E.

6. Any other business

As identified in the Agenda, David Paton asked the participants if anybody wished to take over the role of Network Secretariat. There were no nominations during the meeting and participants were asked to contact OIE/FAO in the next week if they wished to be considered for this.

David Paton mentioned that he had been invited to the SCAD meeting at OIE headquarters in October 2008 to report on the Network.

It was provisionally agreed that the next meeting should be around September 2009 and Divakar Hemadri, India kindly offered to host it.

John Bashiruddin and David Paton
October 2008

Annex A

OIE/FAO
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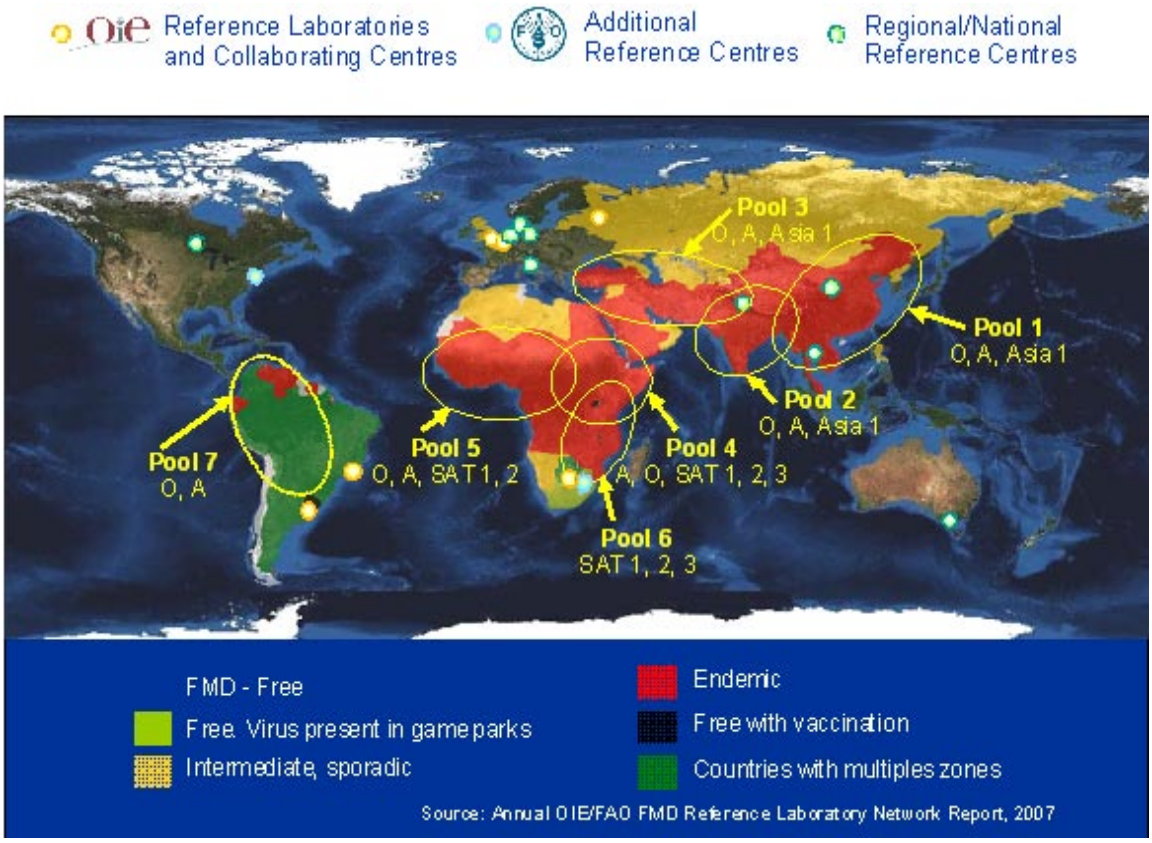
The Watershed Concept



"Global FMD pool is made of mostly separate 'regional' pools here collected into 7 pools based on the circulation of topotypes. Each pool has antigenically distinct virus strains and each distinct virus strain exists normally within a defined region separated by a 'watershed'.

There is continual virus circulation and evolution within regional pools. Therefore each region requires appropriately adapted vaccination programs. There are epidemic jumps between pools and to free regions.

A regionalized control strategy requires long term plans for each regional virus pool where regionally coordinated programs addressing distinct virus strains would need to be considered. Therefore seven 'Regional Roadmaps' that address different starting points, different capacities and different constraints are needed."

Annex B

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Conclusions from Working Groups on Vaccines

Working Groups were asked to assess the position of 'watersheds', list the vaccine seed viruses appropriate for each pool and its vaccine priority in 2008 and to consider what additional work is needed to improve these priorities and for better FMD control.

Group 1 – Pool 1; Group 2 – Pool 2 and 3; Group 3 – Pool 4, 5, 6; and Group 4 – Pool 7 (see Annex A).

Group 1

Members: Thailand, China, Japan. Reported by WL.

Position of watershed: Malaysia and all of Vietnam should be included in the region of Pool 1.

Vaccine seed viruses: Japan – type O was seen as the greatest threat and O Manisa and A Malaysia 97 would be appropriate emergency vaccines.
Thailand – types O, A and Asia1 are current and vaccines O 189/87 (equivalent to O Manisa), A 118/87 (equivalent to A15 Bangkok and A Malaysia 97), and Asia 1 vaccine are appropriate.
China – types O, A and Asia1 are current and local vaccines O 1999 (equivalent to O Manisa), A 1972 (equivalent to A22 Iraq), and Asia1 2005 (equivalent to Asia1 Shamir) were used.
Vietnam – types O, A and Asia1 are current and local vaccines equivalent to O Manisa, A Malaysia 97 and Asia1 Shamir were used.
Malaysia – vaccine to types O, A were appropriate.
Myanmar – type O and a local vaccine equivalent to O Manisa was used.

Priority Vaccines: The priority vaccines were O Manisa, A Malaysia and Asia1 Shamir but the priority for vaccine development was to find a new type O strain that correlated better to the Cathay topotype. It became apparent that there was a 'Cathay' vaccine seed but no further details were offered.

Improvement in Priority Setting: Improving communication between countries of this region was desired. Better surveillance may be needed in some areas, e.g. Myanmar.

Group 2

Members: Russia, India, Belgium. Reported by KdC.

Position of watershed: The geographical positioning of Pools 2 and 3 mainly reflected differences in the A types circulating in there areas.

Vaccine seed viruses: Type A. In Pool 2, Genotype VII has replaced Genotype VI after co-existence for several years (1999-2003). The Genotype VII virus is clearly different from A Iran 05, which occurs only occasionally. In December 2008 A/IND 40/2000 (Genotype VII) will replace A/IND 17/1982 (Genotype VI) in the vaccine.
In Pool 3, the Russian vaccine strain A22 550/USSR/65, which is closely related to A Iraq 64, was replaced in the 90s by A Armenia 98 (A Iran 96 strain) and used until 2006/7, and will now be replaced by A Iran 2005 (A/Turkey/1 2006) for Transcaucasia. The latter was based on laboratory results (sequence and r1 values) and on field results and cross protection challenge tests (vacc. A22/challenge A Turkey 2006). The vaccine for the Far East still contains A22 or a bivalent vac with Iran 05 and Iraq 64.
Type O. In both pools the old O Manisa related strains (O/IND R2 75 in Pool 2; O 1618 in Pool 3) are replaced by more recent O PanAsia 1 related strains based on lower r1 values of O Manisa with currently circulating strains. In future O PanAsia 2 might replace the current strains in the vaccine. In theory could use same type O vaccine strain in both regions.

Type Asia 1. The old Asia 1 strains present in the vaccines (not Asia 1 Shamir) (Asia1/IND 63/72 in Pool 2; Asia1-48/RUS in Pool 3) still provide good protection against currently circulating strains although they are genetically quite different. The Asia1 Shamir vaccine strain might also protect but there is no information about it.

Priority Vaccines: The priority vaccines were O PanAsia (O Manisa or equivalent for now), A Iran 05 type (Pool 3), A IND 40/2000 (Pool 2), Asia 1/IND 63/72 (Pool 2), Asia1-48/RUS (Pool 3) – theoretically Asia 1 Shamir.

Improvement in Priority Setting: The criteria for replacing a strain in a vaccine are apart from laboratory and field data also the considerations whether the strain is widespread and if the new strain remains for some time (more than 1 year).

Group 3

Members: South Africa, Botswana, WRL. Reported by GT.

Position of watershed: Kruger National Park in South Africa should be included in Pool 6; the areas of Pools 4 and 5 are fine, but insufficient information is available on central Africa to define border between 4 and 5.

Vaccine seed viruses: Many vaccine seed viruses have been developed over the years, but not all are still in production. The listing of African vaccine viruses given below is probably incomplete:

Type O – O Manisa, O Uganda, O Egypt, O Kenya

Type A – A Zambia, A Eritrea, A Kenya, A Egypt .

Type SAT1 – SAT1 Kenya, SAT1 RHO 02/78, SAT1 BOT 01/77, OVI: KNP/196/91, SAR/9/81

Type SAT2 - SAT2 ZIM 07/83, SAT2 ZIM 06/95, OVI: ZIM/7/83, KNP/19/81, SAT2 Eritrea, SAT2 Saudi Arabia, SAT2 Kenya (x3), SAT2 Nigeria. SAT2 Zambia

Type SAT3 – SAT3 Zimbabwe (a2), OVI: KNP/10/90.

Priority Vaccines: Not all of the above-mentioned vaccine strains are in production, mainly in southern Africa and there are major problems in finding new strains suitable for vaccine production. This is not only due to the lack of availability of field isolates and sera for use in vaccine matching tests, but also the fact that prospective vaccine strain adaptation for production purposes is a cumbersome process.

Improvement in Priority Setting: There needs to be a systematic analysis of the viruses circulating and their r1 values with respect to current vaccines. There needs to be a survey of the FMD vaccines in production in Africa. Care should be taken on vaccine selection. Improved control measures such as routine vaccination and strict control of animal movement is very important

Group 4

Members: USA, PANAFTOSA, Argentina. Reported by IB.

Position of watershed:

Vaccine seed viruses: Different matching requirements for prophylactic and emergency vaccination. Vaccine strains in current use are O Campos, A24 Cruziero, C3 Indaial and A 2001, Depending on the countries needs bi-, tri- or tetra-valent vaccines are used.

Priority Vaccines: The priority vaccines are as above. Model based on the use of high quality vaccines including broad antigenic strains over the use of multiple strains that give an exact match. Each vaccine batch is thoroughly checked by National authorities. Many countries implemented surveillance strategies to evaluate the efficiency of the vaccination programmes.

Improvement in Priority Setting: No needs detected.

Annex C

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

Conclusions from Working Groups on Surveillance

Working Groups were asked to list the problems affecting decisions on vaccine use, cost effective actions (What to do?) and where the effort should be focused to increase surveillance in the region as described by the 'Pools' (see Annex A).

Group 1 – Pool 1; Group 2 – Pool 2 and 3; Group 3 – Pool 4, 5, 6; and Group 4 – Pool 7 (see Annex A).

Group 1

Members: Thailand, China, Japan. Reported by WL.

Problems affecting decisions on vaccine use: The area was divided into two: (a) FMD free countries i.e. Japan and Korea, and in these countries vaccination may be used primarily to control an outbreak. These countries have a stamping out policy for FMD control; (b) in countries with FMD such as in South East Asia and China vaccination is the primary means of FMD control. However if an exotic strain of FMD was detected stamping out would be used to control the outbreak. Discussion over whether sufficient samples received from all affected countries – e.g. Myanmar?

What to do? In countries with FMD the continued routine biannual vaccination with high coverage was sufficient. China has 100% coverage and Thailand 80% coverage.

Focusing of surveillance efforts: Boundary areas between countries need to collaborate and exchange information and to have regular meetings and to establish training programmes. For example, the OIE SEAFMD Control Campaign has established Upper and Lower Mekong Working group on Animal Movement and Management and The Malaysia-Thailand-Myanmar Project on establishment of FMD Free zones in the Peninsula.

Group 2

Members: Russia, India, Belgium. Reported by KdC.

Problems affecting decisions on vaccine use: (1) Decision makers that lack understanding of the WRLFMD recommendations concerning priority of strains (2) influence of vaccine companies in Decision makers' decisions related to prejudiced choice of vaccine strain (3) lack of information and (under-) reporting from regions and lack of sending samples (4) lack of information/knowledge how to send samples.

What to do? (1) Provide incentives e.g. free vaccine/training in exchange for information (2) provide transport media and training (3) stimulate local laboratory networks (to be promoted by OIE) and local collaboration with veterinary services (4) regionalise FAO/OIE guidelines for strain prioritization.

Focusing of surveillance efforts: (1) concentrate on blind spots (i.e. countries without information), (2) also intensify testing in countries around blind spots, use of NSP surveys to identify incidence levels and areas at risk.

Group 3

Members: South Africa, Botswana, USA, WRL. Reported by BB.

Problems affecting decisions on vaccine use: There were two different scenarios: (a) In Southern Africa control schemes are in place, because of EU export regulations; more data is available for genetic characterization and antigenic matching, more samples are received from surveys and outbreaks. (b) for the rest of Africa – there are less stringent control schemes due to limited or no export of products. This complicates the control of FMD as borders may not be fenced and frequent movement of livestockoccurs in these regions. Situation in the horn of Africa may be starting to change because of pressure from neighbouring Middle Eastern countries e.g. Egypt.

What to do? (1) More systematic work is required, such as recent studies performed where viruses are genetically characterised and compared and r1-values determined by VNT compared. More samples are needed, not only sera but samples for virus isolation. (2) Get local input from different regions to better understand the limitations in the laboratories' capacities to assist in surveillance and why countries are not involved. (3) Local collection/characterisation projects should be initiated. Funding for collection of samples e.g. vehicles for field work is necessary. Projects should be initiated in regional laboratories with PhD studentships for characterization of samples from their countries (this has proved to be very successful in the past). (4) Establish a regional FMD lab in W Africa (French speaking?).

Focusing of surveillance efforts: Surveillance should be on a regular basis. A local lab should assist to know what is going on in the region. Focus should be West and Central Africa. First priority is from where there are no recent isolates i.e. DRC, Angola, Nigeria. Tanzania; second priority is the Horn of Africa (Sudan, Eritrea, Ethiopia).

Group 4

Members: PANAFTOSA, Argentina. Reported by IB.

Problems affecting decisions on vaccine use: In South America where control programmes exist, vaccination has been effective in controlling FMD. More vaccine matching studies for strains circulating in the endemic areas are needed to establish the usefulness of changing (updating) vaccine strains, particularly for emergency situations. Some gaps from endemic countries and difficulties in sending samples.

What to do? Improvement of sample collection by strengthening veterinary services e.g. in Venezuela and Ecuador, especially encouraging political decision makers, involving private sector, and all levels of professionals (epidemiologists, laboratory workers, statisticians).

Focusing of surveillance efforts: Promote surveillance in the well known risk areas.

Annex D

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

Headline information for the Network Report 2008

Pool 1 – To date there have been 2 outbreaks of FMD in 2 separate provinces in Northwest China, both were Asia1. The first was in February in a village in Yingbake, Artux, Xinjiang near the border with Kyrgysztan. Both sheep and cattle were affected. The second was in March in Qutou, Pinglao, Ningxia, Only cattle were affected. In 2008 the RRL in Pakchong, received 32 samples from Thailand 16 of which were type O, 7 were type A, and 9 were not typed. For type O, r1 values of >0.4 were obtained with O 189/87 and for type A >0.4 with A 118/87. RRRL also received 11 samples from Lao PDR and all were Type O and gave r1 values of >0.4 with O 189/87.

Pool 2 and 3 –In India the ME-SA topotype of type O is most often the cause of FMD outbreaks, A and Asia1 account for the remainder. The O PanAsia II strain, PanAsia I and IND 2001 co-circulate with PanAsia II predominating. Genotype VII is the sole strain causing outbreaks of type A. However, since 2006 some strains of the same genotype with a deletion at amino acid position 59 in VP3 has emerged and is predominant. Outbreaks in the eastern region were caused by Asia1 of lineage CI that has re-emerged since 2005. Information collected by ARRIAH showed O PanAsia II in Central Asia. Vaccines included: for type O PanAsia I and/or combined with O Manisa; for Type A, a strain related to Iran 05 and for Asia1, Asia1/Georgia/2001 for Transcaucasia and an Asia1 from China used in the buffer zone in the far East. According to WRL the Middle East has type O PanAsia II and type A in Turkey and Iran.

Pool 4, 5 and 6 –

Pool 7 – In Notre de Santander, Columbia, near the border with Venezuela outbreaks of type O and A were recorded in Cucuta and Sardinata, respectively. Viral detection was a result of a follow-up of NSP positive animals during routine surveillance. Both episodes were effectively controlled.

Annex E

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

Conclusions from Working Groups on Network Priorities

Group 1

Members: Thailand, China, Japan. Reported by YL.

1. Efforts should be made towards the creation of a subgroup or working group of East Asian FMD Reference Laboratories that focuses on China, Hong Kong, Japan, Korea, and Taiwan.
2. The OIE/FAO FMD Ref Lab network should continue working on interlaboratory comparative vaccine matching exercises.

Group 2

Members: Russia, India, Belgium. Reported by NG.

1. The Project Directorate on FMD, Indian Council for Agricultural Research will have additional functions as SARC Ref Lab in near future. As such they will perform some exploratory work on what is available in the region in terms of samples, reagents, test methodologies etc
2. On the topic of vaccine matching, the group recommends to include more laboratories for the next collaborative study phase (e.g. Brazil, Argentina, Germany, Belgium etc). The group further recommends to repeat the serotype A study (before moving on the serotype O for which preparation could nevertheless commence) giving the participating labs the opportunity to improve their assays (several labs openly stated to have little or no experience with r-value determination prior to the study). The question of who is right and who are wrong remains. Moreover, what is the "gold standard" test [vaccine matching by serology (VNT or ELISA using a harmonised test protocol) versus in vivo cross-protection]. Would it be possible to include sera from recently performed cross-protection studies (e.g. Brehm et al., 2008; Goris et al., 2008) thereby extending the panel used in the present study? Maybe even the option of jointly performing additional cross-protection studies within the Network should be considered? The future aim should be to hold a PTS for r1-values after having levelled the playing field among participants.
3. The group also requested to perform collaborative studies on other test methodologies such as VI, PCR, Ag-ELISA, Ab-ELISA, NSP testing (also the aspect of NSP-freedom of vaccines) and VNT. Does one size fit all or should we have more tailored assays for different regions in the world?

Group 3

Members: South Africa, Botswana, WRL. Reported by BB.

1. Initially, workshops for the SADC region should be conducted to identify the capacities of laboratories within the region, to take an inventory of positive sera available for proficiency testing, to have a group that focuses on SAT types. Funding for the collection of sera for this purpose should be sought.
2. The export driven countries are better established compared to other countries that are less able. Therefore, Botswana, South Africa and Namibia could be part of a bigger network for proficiency testing, where not only the SAT serotypes are tested.
3. A person or committee from this region should be identified to provide structure for these exercises.
4. A second workshop should include other laboratories from East/West Africa as well as SADC countries.
5. Vaccine matching focussing on SATs should be instigated with one outside (European) laboratory involved. (WRL expressed strong interest in being involved.)

Group 4

Members: USA, PANAFTOSA, Argentina. Reported by SM.

1. Further vaccine matching inter-laboratory trial would be most appropriate because the NAVB is doubting/questioning the meaning and usefulness of r1 values.
2. There should be a framework for the exchange of reagents and viruses (perhaps controlled by an MOU).
3. There should be an inventory of assay development projects within the Network laboratories.
4. The Network should keep in touch with periodical conference calls as well as the annual meeting.

Annex F

Other Observers

Zhidong Zhang and Yanmin Li, IAH, Pirbright, UK and staff from thr LVRI provided translation support.

Many observers attended this meeting from National FMD Laboratory, Lanzhou Veterinary Research Institute, Gansu, China.

Junwu Ma	Xiaoyan Shen
Yonglu Wang	Guangxian Wang
Dong Li	Jinyan Wu
Zengjun Lu	Junjun Shao
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Yimei Cao	Junzheng Du
Pinghua Li	Tong Lin
Xinwen Bai	Shandian Gao
Pu Sun	Guohua Wu
Yuanfang Fu	Xinmin Yan
Meina Tian	Yongsheng Liu
Yamin Yang	Haotai Chen
Yongjun Shang	Mi Lin
Hong Tian	Shunyun Qi
Yanyan Chang	Guangqing Zhou
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