REPORT
of the
OPEN SESSION
of the
STANDING TECHNICAL COMMITTEE
of the
EUROPEAN COMMISSION FOR THE CONTROL OF FOOT-AND-MOUTH DISEASE
(EuFMD)

Held in
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29 September-1 October 2010

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The generous support of our **sponsors** has greatly assisted to reduce the cost of hosting the Session, and of registration, thereby enabling wider participation, and is greatly appreciated.

- DG-SANCO
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- Merial
- Prionics

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OPEN SESSION OF THE EuFMD RESEARCH GROUP

Considerations and Recommendations of the Open Session

Considering that:

1. There is a need to improve information flow between field, laboratory, and disease management teams, national and internationally, to enable each level to better identify the significance of disease and virological patterns;
2. FMD free countries and those in endemic regions need to identify suitable vaccines/antigens for their emergency and preventive programs, but there is a lack of standardized framework or approach to deal with the uncertain incidence in endemic regions and risks of introduction, and to the level of cross-protection to be expected, and the duration of benefits of change in seed viruses;
3. To progress along the **Progressive Control Pathway** (PCP), countries are required to provide evidence of application of activities involving monitoring and surveillance of FMD and on the application and impact of control programs. To generate such information, countries are challenged with the issue of designing complex surveys;
4. Value/market chain analysis methods are means to identify critical FMD risk points in affected (and at risk) countries, building upon more traditional epidemiological and virological approaches;
5. In the last three years the PCP approach has been used in several parts of the world, and greater confidence in the results of stage assessment could be achieved with further definition of the requirements in each stage, and of the system for verification of control activities (particularly the requirement for release of results);
6. The dynamics of emerging FMD epidemics have usually been defined by molecular typing, but structured field investigation will provide a wider range of information and should not be overlooked;
7. Most countries in Subsaharan Africa are at PCP level 0 or 1;
8. Most countries have national reference laboratories (NRLs) for FMD but there are no Reference Centers (RCs) recognized by FAO or OIE within virus pools 4 and 5;
9. The economic and political importance of FMD appears to be increasing, but the economic assessment of control options has yet to be systematically undertaken in most countries;
10. Prerequisites for efficient control include early warning and early detection, rapid and efficient response measures, and national capacity to inform and assist decision makers based on a well tested combination of local and national expertise and validated models.

Recommends that:

Regarding recommended antigen strains maintained in vaccine banks

1. Greater effort is placed by the international organizations to integrate the virological typing data such as generated by the World Reference Laboratory (WRL), with information from official and unofficial sources as a result of regional projects and programs; this effort should include greater integration and support for FMD networks and laboratories connecting NRLs in each virus pool;
2. Development and evaluation of the model for ranking the risk posed by viral pools be continued, but it must be ensured that the limitations and assumptions are clearly identified and communicated with the results; both the ranking system and the results of virological assessments should be presented to the next EuFMD Commission Session;
3. More effort should be placed on integrating intra-regional animal movements information with other layers of risk information, to better assess risk associated with new virological findings;
4. Strain recommendations for inclusion in vaccines should be risk based, as well as taking account of international and regional vaccine availability and vaccine matching data;
5. To improve vaccine selection and stimulate the development of more cross-protective vaccines, research should be directed at understanding the repertoire and mechanism of action of the polyclonal antibody response as well as defining the protection associated with different paratopes;
6. International cooperation between vaccine producers and reference laboratories should be encouraged to help overcome problems in availability and access to vaccine matching reagents, i.e. vaccine strains, sequence data, field isolates and antisera; FAO and other vaccine purchasers should place conditions on suppliers to provide suitable reference reagents, or fund their production by independent laboratories, to ensure the vaccine matching system is sustainable;
7. Studies to better characterize and improve the reliability of vaccine matching methods should continue to be supported, not only for current vaccine selection but also for development of new in vitro and computer based (*in silico*) selection processes;
8. A fuller understanding is needed of the antigenic diversity within some serotypes and regions and of the significance that this has for vaccine induced protection. The EuFMD Research Group should assess the gaps in knowledge and their relative importance;
9. A more systematic approach should be developed and used to evaluate vaccine effectiveness in the field, and report made summarizing current studies and options, to the next Research Group Session.

Regarding vaccine control

10. In process control methods, for quantification of FMD-NSPs in vaccines should be further validated; if used by FMD vaccine producers, methods and results should be published when part of their claim for purity;
11. Indirect assessment of FMD vaccine potency and vaccine matching should be harmonized to obtain exchangeable/comparable results by close co-operation between vaccine producers and international FMD reference laboratories;
12. Antigen stability should be given greater priority in quality control, and standards and associated tests to measure stability should be further developed and validated by both vaccine producers and research laboratories.

Regarding antigenic diversity, vaccine selection and monitoring

13. Greater efficiency in the identification of significant variation in FMDV could be achieved through optimizing use of regional and world reference laboratories services; flowcharts describing sampling procedures could be agreed, covering sample selection, tests at national and regional level, and when to send samples to reference laboratories for advanced typing;
14. The EuFMD/FAO should support initiatives that connect NRLs and International Reference Centres (IRCs) to achieve greater efficiency in application of molecular typing, using protocols which meet the quality standards of the FAO RCs;
15. More should be done to investigate the performance of vaccines in the field as this may differ from what was found at the point of manufacture for reasons such as vaccine stability. Greater application of vaccine effectiveness measurements are needed, comparing the risk of disease in vaccinated animals to the risk of disease in non-vaccinated animals. Different vaccination regimes could also be compared to identify optimal strategies.

Regarding the Progressive Control Pathway for FMD in practice

16. That the EuFMD Working Group on the **Progressive Control Pathway** (PCP) guidelines be further expanded to involve those epidemiologists with expertise in design of surveillance programs, and who are working on FAO or other PCP support projects, to learn the lessons from application, to further develop practical guidelines, and standards for surveys and analysis of data;
17. FAO is encouraged to further develop the market chain analysis approach and promote its use and integration in the framework of PCP/Roadmaps;
18. FAO and OIE are encouraged to further define requirements for each stage, make them verifiable and consider the possibility of some form of PCP status acceptance;
19. Support necessity of cooperation of EU, OIE and FAO on the PCP.

Regarding diagnostics

Concerning pen-side tests

20. Information regarding performances of Lateral Flow Devices (LFD) for FMD antigen detection should be systematically collected, and guidelines developed for dealing with uncertainty (interpretation of weak results, false positive detected in the field, if any);
21. LFD for serotype-specific detection should be developed, and if the commercial market is uncertain, international organizations should consider taking the lead to commission LFD for field evaluation (EuFMD/FAO/EC);
22. Research on development of other pen-side tests for antigen detection based on alternative methodologies, such as dry ELISA, is encouraged;
23. Continued development of high sensitivity (better than LFD) and high speed (similar to LFD) penside tests using genome amplification methods are recommended;
24. Guidance on the use of pen-side tests should be updated, particularly regarding use in countries without a national reference laboratory capable of alternative confirmation methods, should be established.

Concerning genome detection

25. Given the wide variation in protocols applied for RNA extraction and RT-PCR, it is recommended that countries make greater use of the protocols validated at the WRL (for both Real Time and classic RT-PCR); the SOPs on the WRL Web site should be used;
26. Diagnostic development priorities should be:
    i) Development of ready-to-use kits for RT- PCR, similar to those already commercially available for other TADs;
    ii) Development and validation of serotype-specific RT-PCR;
    iii) Development and validation of multiplex RT-PCR appropriate for regional settings (as serotypes and strains differ).

Concerning Antigen detection and typing ELISA

27. Ready-to-use kits should be commercialized and the international organizations, representing buyers, should become early adopters for evaluation and to encourage sustainable supply.

Concerning immunoassays for antibody detection

28. Ready-to-use kits for SP antibodies should be further developed, validated and made available;
29. The WRL should make available on demand a cost recovery basis:
    i) International serological standards for Asia-1, SAT types, and for relevant antigenic variants (type A);

ii) Proficiency panels for calibration and evaluation of in-house assays, and for batch control;

30. The EuFMD Research Group should work on guidance / recommendations for use of Solid Phase Competition ELISA compared to the Liquid Phase Blocking ELISA.

Concerning QA/QC

31. FAO or the Research Group of the EuFMD should develop guidance on the minimum standards for QA/QC for laboratories performing services required for the different Stages of the PCP.
32. Diagnostic test producers should make available validation dossiers, for accreditation according to ISO17025.

Concerning new developments

33. Multiplex tests: priorities are a multiplex PCR with sufficient sensitivity, but also there should be attention to multiplex detection of FMD antigens and antibody, and greater use of recombinant antigens (VLP; universal ligands, etc).

Regarding FMD epidemiology – Eurasia and South America

34. Greater attention must be made to training in disciplines needed to rapidly assess "What is the impact on animal health? What are the possible routes of transmission and what are the socio-economical effects?". This information is necessary to identify and address the critical control points in the PCP, and is helpful to feedback to field veterinarians to support their activities in controlling FMD;
35. The time delay between disease event and results of molecular typing must be shortened to a few days, in order to support decision making in complex epidemic situations. Support should be given to use the power and throughput in high technology laboratories to test samples rapidly or transfer technologies to Regional RCs and NRLs in affected areas.

Regarding FMD epidemiology – Africa

36. International organizations should support countries in Sub-Saharan Africa to initiate PCP Stage 1 activities. Training of regional experts in PCP could assist to build confidence in design of activities, such as sero-surveillance and epidemiology and socioeconomic assessments needed to develop country strategies;
37. EuFMD or FAO should strengthen regional laboratories to support primary diagnosis in NRLs in West/Central and Eastern Africa.

Regarding Control of FMD in free countries

38. EuFMD reviews the use by countries of decision support systems, including models, in developing and testing their contingency plans for a variety of scenarios of disease introduction, and explore the impact of different control measures;
39. More research is conducted on the likely intra-community spread of FMD if introduced at different times and locations into the EU;
40. The continued development of expertise in FMD recognition and immediate response, but ensuring that laboratory veterinarians as well as field veterinarians are trained from each state, since they will need to work together to ensure rapid diagnosis and to establish surveillance;
41. Continued support for work to identify contact rates and critical points for transmission, with a view to develop practical methods for application in contingency planning or during the early epidemic response.

Regarding FMD training

42. Trainees from the *Real Time Training Courses* become, as far as possible, trainers in their own countries;
43. Better preparation for the training by the trainees would improve the team work and contribution to final output;
44. Refresher courses and workshops should be organized and update the trainees on developments; and that modules for additional FMD experience should be considered (outbreak management, use of decision support models, etc).

REPORT

Open Session of the Research Group, 29 September-1 October 2010

The Open Session of the Research Group of the Standing Technical Committee of the EuFMD was held in Vienna, Austria, from 29 September to1 October 2010, with the theme "**New tools and challenges for progressive control**". The Session was attended by over 240 participants from across the world, predominantly from Europe and Africa, but also with good participation from East Asia and South America. The program was organized into fourteen technical sessions, covering recent advances and ongoing technical constraints affecting *progressive control of FMD.* The Session considered six keynote papers and 82 presentations, relating to the 14 items. One evening debate was held, and forty-two posters presented. Two panel discussions were included in the program, one concerning the control and monitoring of vaccination and another with private industry representatives.

The Agenda of the Session is **Appendix 1** and the list of participants in **Appendix 2**.

Opening

The Session was opened by Dr. Sonja Hammerschmid, Rector of the University of Veterinary Medicine, Vienna, who reminded the participants of the long history of teaching and research in Vienna, from 1765. Control of infectious diseases had always been a major importance in Austria, being situated in the European landmass and at risk from sweeping epidemics arriving from far and near. Veterinary schools have an important role to ensure that the next generations of veterinarians have an understanding of their role, which can be crucial for early recognition and response.

Dr. Ulrich Herzog, CVO Austria and Chairman of the EuFMD Executive Committee, welcomed participants to Vienna; he was glad to see that several networks and projects had used the opportunity to organize side meetings, and trusted that the Open Session would not only a great scientific success but assist experts to work together in new ways and with new ideas. He considered the Open Session of major international Importance and looked forward to receiving ideas and views on how the role as a forum and meeting point could assist in further international collaboration on FMD science. He declared the meeting open.

Two plenary presentations were then given, one being the Frenkel Lecture, and the other on the management of the recent type O incursion into Japan in 2010.

Day 1

Frenkel Lecture

The main Plenary Lecture at the Open Session is named after the renowned Dutch scientist whose "Frenkel method" introduced the first possibility of mass vaccine production and application in the world.

The Lecture "*Integrated procedures to assess FMD vaccine quality and herd immunity in Argentina*" was presented by Dr. Jose La Torre (Argentina). This paper described the development of the scientific basis for current control of vaccine quality and potency, and of the vaccination programme monitoring, which have been a major part of the improvement in success of vaccination for the control of FMD in Argentina. The lessons learnt, he proposed, should be understood and applied in other regions where vaccination is to play the principal control measure in preventing virus circulation (**Appendix 3**).

Control of FMD in Japan

Dr. Toshiyuki Tsutsui presented a paper on "*The FMD disease epidemic in Japan, 2010*", which described the evolution and progression of this incursion which proved extremely challenging for control, and resulted in massive costs for the sector and Government, with stamping policy changed to vaccination during the crisis, which was followed by culling of vaccinated animals. Japan is a country that is usually FMD-free, and the area most affected was densely populated with pig, dairy and beef farms. He described some of the challenges encountered when implementing control in this area. (**Appendix 4**).

Progressive control of FMD - in practice

The Session introduced the **Progressive Control Pathway** (PCP) for FMD, which was first developed by EuFMD together with FAO projects at a workshop in November 2008 for development of Long Term Regional approach to FMD control in West Eurasia. The issues considered included: What have we learnt from applying the PCP approach in West Eurasia in 2008-10?. After national sero-surveys for FMD, is there a smart alternative to national vaccination campaigns in all species? Are the guidelines for monitoring and surveillance, and for lab capacity in each country, appropriate? How do we identify

critical control points, and bring in socio-economic assessments to identify how and what can be done better?

This first session began with a keynote addressed by Dr. Keith Sumption, Secretary of the EuFMD Commission (**Appendix 5** and **Appendix 5b** is the paper presented to the Paraguay conference on "*PCP and regional roadmaps towards a common framework for long-term action against FMD at national and regional levels*"). Dr. Kris de Clercq, representing the OIE, then described the work in progress on the relationship between the PCP Stages and the OIE Standards (**Appendix 6**). Further presentations illustrated the experience of applying the PCP to country situations, including design of surveys to achieve Stage 1 (Dr. Ferrari, **Appendix 7**), the monitoring of vaccination and control measures (Dr. Yadin, **Appendix 8**), the progress from zonal Stage 3 to official recognition of freedom under vaccination in Thrace (Dr. Potzsch, **Appendix 9**), and the activities needed to maintain freedom (Dr. Füssel, **Appendix 10**).

FMD risk assessment, threat detection

Issues in this section were: How do we quantify/prioritize the threats from each virus pool to Europe? How can we better use regional networks to give us "viral intelligence" on emerging threats? Can we predict epidemics within West Eurasia, based on long term monitoring and viral characteristics? What viral predictors could be used? How do we get closer to real-time information on FMD events? Does risk information change lead to any difference by national risk managers (e.g. to the Far-East type O epidemics in March/April 2010)?

This session featured a keynote presentation from Dr. Jef Hammond, Head of the FAO WRL for FMD, Pirbright (**Appendix 11**). This was followed by presentations considering if FMD epidemics can be predicted (Dr. Bulut, **Appendix 12**), on risk of FMD incursions from different regions to Europe (Dr. McLaws, **Appendix 13**), on the genetic basis of the type A epidemic development in Turkey (Dr. Ozyuruk), and the further development of the FMD BioPortal (Dr. Pérez, **Appendix 14**).

Session on Vaccine Development and Vaccine control

Developments in vaccine development and immune response to FMDV were presented p (**Appendices 15-19**) and four of these papers involved work with different approaches (reverse genetics and expression systems) to genetically engineer FMDV.

Seven papers on control of vaccines and vaccination programmes were presented (**Appendices 20-26**), covering important developments in emergency vaccine formulation procedures, work to

improve thermostability, indirect assessment of potency, serology for herd immunity, in process controls for NSP in vaccines, and effect of thiomersal on FMDV virions.

Antigenic diversity, vaccine selection and monitoring

This session was organized by the antigenic diversity and vaccine selection working group, under the EuFMD Research Group, led by Dr. David Paton. The Issues: How can we improve the guidance (cross-protection, antigenic relevance) to vaccine bank managers on which antigens to hold for the current risks?. What do new approaches (such as Antigenic Cartography) offer? How will these methods change our working practises in global viral threat identification and in countries using vaccination? Why do we seem to have a problem with type O vaccination, when type O is relatively antigenically stable?

This session opened with a keynote presentation by Dr. David Paton (**Appendix 27**), followed by seven further presentations on antigenic diversity and methods to estimate antigenic relatedness and cross-protection, including progress to predict from sequence data, the use of serological data, including in antigenic cartography, and cross-protection studies between type O (Manisa and Campos). (**Appendices 28-34**).

Day 2

The Progressive Control Pathway for FMD; Papers on lessons learnt from practice

Six papers were presented in this session that described approaches to surveillance, economic considerations and FMD control within the PCP framework. The first two (Dr. Ferrari, FAO, and Dr. Bartels, EuFMD) considered design of surveys needed for risk assessment (PCP Stage1), followed by papers on methods for improving the identification of control measures in the market chain with socio-economic assessments, and on implementing the PCP approach in Ethiopia and the TransCaucasus (**Appendices 35 to 40**).

Monitoring Control and Vaccination Programmes Session and Panel

Two papers were presented in this session that described different approaches to evaluate vaccination at the herd level (**Appendices 41-42**). This was followed by a panel discussion.

FMD molecular characterization

This session comprised six presentations relating to advances in the molecular characterisation, starting with an overview on definitions and nomenclature given by Dr. Nick Knowles (**Appendix 43**), followed by presentations on applications and advantages of full FMD genomic sequencing when applied to understanding big epidemics and localised spread between and within herds (**Appendices 44-45**). The potential of next generation sequencing was presented by Dr. Caroline Wright (**Appendix 46**).

Diagnostics

This session was organized by the *Diagnostics Working Group* of the EuFMD Research Group, led by Dr. Emiliana Brocchi.

Issues: FMDV nomenclature: proposal for new system. Test validation – what's new, what are the gaps? What are the gaps in our diagnostic repertoire? Which diagnostic tests are needed at each PCP Stage, from endemic to near-freedom? What are we gaining from Full-Genome sequencing to guide diagnostics?. How do we rapidly type FMD to strain level, in affected West Eurasian countries?. Can we

profile herd infection using diagnostics, to identify how long infection has been in a herd? Carrier status of domestic buffalo.

This long and important session considered a keynote presentation (Dr. Vilna Wosloo, **Appendix 47**) and 11 papers concerning the detection of FMD virus, antigen and antibodies (**Appendices 48-58**). These papers covered important developments that could lead to preserved RNA rather than live virus being transported for reference centre typing, with use of transfection to recover live virus (project supported by EuFMD); the development of simple ELISA for antigen detection, the evaluation of penside tests, and comparison of rapid one-step RT-PCR assays. Global and regional harmonization and proficiency testing operated by WRL (for FAO and the EC) and regional examples (for SADC) were presented.

FMD epidemiology

Issues: What have we learnt on why, when, how epidemics or outbreaks occur? Risk based surveillance: experience and guidance. Surveillance in vaccinated populations: Still a problem with impure vaccines? What have we learnt from epidemics in free countries in 2010?.

– *Eurasia and South America:*

This Session consisted of 11 presentations on the epidemiology of FMD in Eurasia and South America (**Appendices 59-69**). These papers highlighted the resurgence of interest in FMD epidemiology, and in the move beyond molecular studies into understanding contact networks and a better description of the space and time dynamics of FMD. These studies fit well with requirements of PCP Stage 1 to define the risk populations and transmission risks.

– *Africa:*

This session included 10 papers related to issues important to FMD in Africa, including results from sero-surveys, molecular and virological studies (**Appendices 70-79**).

Control of FMD in free countries

This session included six scientific presentations concerning FMD preparedness and control in countries that are usually FMD-free (**Appendices 80-85**), highlighting the importance of a using different rigorous testing procedures for evaluation of contingency plans for FMD incursions.

Antivirals and other developments

Five papers were presented in this session (**Appendices 86-90**) concerning FMDV pathogenesis and recent advances in the development of antiviral drugs.

Surveillance technologies

Issues: Mobile phones and FMD: How do we communicate in a quicker and smarter way with those that need to know? Farmer-led reporting: Can we rapidly scale up information flows during a crisis? I-Phones and FMD. New diagnostics; Theoretical or practical? What quality standard must novel FMD vaccines meet for international acceptance?

Two papers were presented in this session, concerning technological and diagnostic technologies relevant to FMD surveillance (**Appendices 91-92**).

FMD Real Time Training and Private Sector Platform

Issues: This session reviewed lessons learnt from training of over 70 persons in FMD recognition and outbreak investigation practices, under the EuFMD/EC real-time FMD Training Program in 2009-10. How do we retain the experience and keep trainees up to date? Do we need refresher events/courses/online exercises, and to extend the experience to include FMD in pigs, etc? The program ended with an open session which included a description of FMD real-time training courses offered by EuFMD in 2010 (**Appendix 93)** and the platform was given to the private sector (representatives from Intervet ,Merial, Prionics and a talk on the Public/Private Sector arrangements in India).

Closure

The EuFMD Commission gratefully acknowledges the support of Dr. Ulrich Herzog, CVO Austria and President of the EuFMD Executive Committee, the local organizing agency AGES, as well as the companies who generously sponsored the meeting.