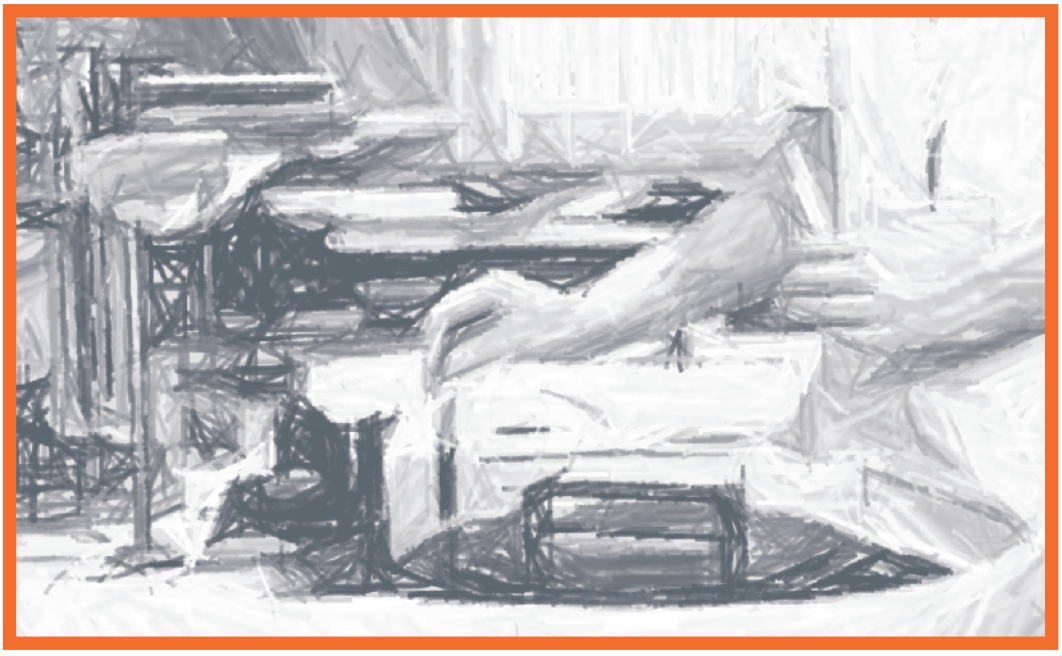
Manual 8

Laboratory support



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World Organisation for Animal Health
12, rue de Prony
75017 Paris, France
Tel.: 33-(0)1 44 15 18 88
Fax: 33-(0)1 42 67 09 87

www.oie.int

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Contents

Background

Laboratory diagnosis is an essential component of any disease control program. Early, rapid and accurate detection of disease is essential for effective control of transboundary animal diseases (TADs), including FMD. For diseases where clinical diagnosis alone is not sufficient to confirm infection, as is the case for FMD, reliable laboratory diagnostics are essential for the purposes of disease control and for safe trade (OIE, 2010). Furthermore, the existence of multiple serotypes and subtypes of FMD, which are clinically indistinguishable, means that identification of serotype and further characterisation into subtypes of FMD isolates is essential to understanding the epidemiology of FMD both locally and regionally. It is therefore important that samples are sent to laboratories with sufficient capacity to rapidly and accurately confirm diagnosis of FMD and, where necessary, perform further characterisation of isolates.

On a national and regional level, early detection and effective disease control depends upon access to expertise and reliable laboratory diagnostic facilities. On a global scale, there is a need for such facilities and expertise to be distributed evenly so that all countries and territories can readily access them (OIE, 2010). The improvement of global laboratory capacity for FMD is supported by a network of OIE/FAO reference laboratories across the world, which is led by the World Reference Laboratory for FMD (WRLFMD) in Pirbright, UK. This global reference laboratory network helps to ensure that FMD expertise and diagnostic services are accessible to all OIE member countries. South-East Asia and China is represented strongly within this network by two OIE-designated Regional Reference Laboratories (RRL): one in Pakchong, Thailand and another in Lanzhou, China. The role of these reference laboratories and laboratory networks will be described in more detail in this manual.

Despite the importance of laboratory diagnosis to FMD control, supported by OIE/FAO reference laboratories and the efforts made to improve capacity globally, the standard of laboratory diagnostics (at the national and sub-national level) remains highly variable. This is likely a result of limited capabilities and/or resources (OIE and FAO, 2012) with shortfalls being most apparent in developing countries (OIE and FAO, 2012; Namatovu *et al*., 2013), and predominantly in those areas where FMD remains endemic. Therefore, it is essential that countries continue to strive to strengthen laboratory capacity in order to improve control of FMD and/or to achieve or maintain freedom from FMD.

Veterinary laboratories should all meet certain minimum standards with respect to: biosecurity/biocontainment; health and safety; quality assurance systems; and suitably trained staff (the OIE Terrestrial Manual of Diagnostic Tests and Vaccines for Terrestrial Animals - referred to hereafter as the OIE Manual; Chapter 1.1.0.). Member Countries seeking to achieve or maintain OIE recognised status for FMD freedom or OIE endorsement of an official FMD control program will need to ensure that FMD laboratories meet the standards detailed in the OIE Manual. For countries where FMD is endemic, laboratory capacity should be assessed, weaknesses identified and plans made to strengthen capacity in those areas. Regardless of the official FMD status of a country, and the legal framework in place, laboratories should maintain at least a minimum level of capacity to ensure that the health and safety of personnel working in laboratories and the safety of livestock populations within the country are protected. The OIE Performance of Veterinary Service (PVS) evaluations represent a valuable method for identifying gaps in laboratory capacity and will be discussed later in this manual. The general considerations for laboratory standards will not be covered further in this manual, but readers are urged to refer to the OIE Manual for further information.

The SEACFMD Campaign covers countries and zones at varying stages of FMD control and eradication, ranging from those countries and zones which are recognised as FMD free (without vaccination), those which have an OIE-endorsed official FMD control program, and countries where FMD is endemic. The role of diagnostic laboratories and the required diagnostic capacity varies with the stage of control and eradication of FMD in each country. This manual outlines the requirements in terms of laboratory diagnostic capacity for countries seeking to achieve or maintain OIE freedom and for those seeking OIE endorsement of an FMD control program. In addition, information will be provided on the progressive control pathway for FMD (PCP-FMD) and the required laboratory diagnostic capacity to progress to different levels within the pathway.

A key resource for this manual is the OIE Manual, and the reader is encouraged to refer to the following sections for further information on the subjects covered in this manual:

- Chapter 1.1.0. Management of veterinary diagnostic laboratories
- Chapter 1.1.3. Biosafety and biosecurity: standard for managing biological risk in the veterinary diagnostic laboratory and animal facilities
- Chapter 1.1.4. Quality management in veterinary testing laboratories
- Chapter 1.1.5. Principles and methods of validation of diagnostic assays for infectious diseases
- Chapter 2.1.5. Foot and Mouth Disease (specific information relating to diagnostic tests and vaccines for FMD)

Laboratory-based diagnostic capacity amongst SEACFMD Member Countries

The two OIE-designated reference laboratories for FMD in the region (RRL Pakchong in Thailand and RRL Lanzhou in China) provide valuable services in the region, as well as making significant contributions to FMD prevention and control through research and development of diagnostic tests, vaccines, training, etc. Further details on the role of reference laboratories are provided in a later section of this manual.

Some of the major gaps identified amongst SEACFMD member countries in terms of laboratory function and capacity during a meeting of the SEACFMD laboratory network in 2014 are outlined in Box 1. Possible solutions to the gaps were raised during the meeting and are included in italics. At the time of writing, SEACFMD Member Countries had started to address these gaps, but many require ongoing effort and will remain relevant throughout Phase 5 of the SEACFMD Campaign. For example, sample submission rates are improving in most endemic countries, but ongoing effort in this regard is important for optimising surveillance and control activities.

The role of diagnostic laboratories for FMD

As described above, laboratories have a key role to play in FMD detection and control, both in countries which are free from FMD and those in which the disease is endemic, albeit that the role of the laboratory can be quite different under these different settings. In countries where FMD is endemic, the laboratory will be involved in: confirming diagnosis of FMD in clinical or suspect cases; active surveillance studies which measure the prevalence of infection/exposure in a given population and help to identify disease hotspots and/or monitor the success of control measures. Where vaccination is used routinely, or where it may be used as an emergency measure, laboratories are essential for post-vaccination monitoring and vaccine matching purposes (see Manual 4).

In FMD free countries, or countries where FMD outbreaks occur only sporadically, diagnostic laboratories form an essential part of an early detection and response system, whereby it is necessary to be able to gain a rapid and accurate

Box 1: Gaps identified in sample submission and laboratory function/ capacity amongst SEACFMD member countries (SEACFMD, 2014)

- Poor quality (and quantity) of samples submitted to the national laboratory
  - Establish a feedback mechanism on quality of samples submitted (for both bad and good samples received).
  - Ensure continued access to (good quality) transport medium by developing a mechanism for regular replenishment of stock transport tubes/buffer.
- Low submission rate to reference laboratories
  - Advocacy to authority.
  - SEACFMD target: Submit at least 30 representative samples/year/ endemic country for characterization.
- Lack of strategic selection of representative samples from the region
  - Relay this gap to the Epidemiology Network
- There is no systematic collation of results of all characterised isolates from the region
  - SEACFMD website (note amendment 33 regarding OIE WAHIS changes)
- There is no established system to link outbreak data/epidemiologic data to characterised isolates

  Develop a system to give a unique identifier to each outbreak and include this identifier in the lab submission form.
- Issue on preparedness of FMD-free countries to identify/confirm FMDV
  - Refine the system of network for submission.
  - Establish at least molecular detection methods.
  - Conduct a scenario-based simulation for FMD laboratories of FMD-free Member Countries.
- Issues on succession plan and fast turnover rate of trained personnel
  - Develop good documentation (for easy turnover).
  - Develop exchange programs for the region.
  - Advocacy to decision-makers/authority.
- There is insufficient number of samples for sero-surveillance for some of the free countries
  - Relay this gap to the Epidemiology Network
- Some of the free countries do not participate in Proficiency Testing administered by RRL-Pakchong
  - Indonesia : explore participation in the WRLFMD PT
  - Philippines : participate in select tests only (NSP)
  - Brunei: participate in select tests only (NSP)
- Lack of corrective actions by laboratories with sub-optimal performance based on proficiency test findings
  - RRL to prepare an easy-to-understand letter to the authority/laboratory, clearly identifying the good and bad findings and list suggestions on ways to improve the performance of the laboratory
- Issues on communication of proficiency test results
  - RRL to send hardcopy to SEACFMD LabNet focal point
  - SEACFMD LabNet focal point to provide RRL the correct and updated contact details for communication
  - SEACFMD LabNet focal point to communicate/disseminate the findings to relevant persons within the country (decision-makers, laboratorians, etc.)

diagnosis for any suspected cases of FMD. It is important that laboratories in FMD free countries maintain capacity to ensure that they can cope with a sudden upsurge in samples in the event of an outbreak (see Manual 11). The list Box 2 outlines some of the key activities of diagnostic laboratories for FMD. Note that not all of these functions may be carried out at National FMD laboratories, but there should be arrangements in place to allow timely submission of samples to laboratories (usually FMD reference laboratories) where additional tests are available.

Box 2: Activities of an FMD diagnostic laboratory

- Confirmation of diagnosis of clinical or suspect cases of FMD
- Trade purposes: pre-import/export testing of consignments and/or individual animals
- Active surveillance studies (demonstrating freedom from infection in defined animal populations, estimating prevalence/incidence of infection; identifying disease 'hot-spots')
- Post-vaccination monitoring
- Monitoring the impact of control measures
- Vaccine matching
- Identifying patterns of spread/source of virus (through sequencing)

Overview of FMD diagnosis and diagnostic tests

In the majority of cases a definitive diagnosis of FMD is based on the demonstration of the presence of FMD virus or antigen. Tests are applied which identify whether or not the virus is present and, if present, to identify the specific serotype. When tissue samples cannot be obtained, diagnosis may be based on the demonstration of FMD specific antibodies in serum samples. However, there are limitations to diagnosing FMD by antibody detection methods in that the presence of antibodies indicates previous exposure to virus (or vaccine) and does not necessarily indicate active infection.

If FMD is confirmed and viral DNA or antigen is available, further laboratory investigations can be conducted, including: detailed antigenic and genotypic characterisation of the virus, so that advice about a suitable vaccine can be provided; and comparison of the field isolate with strains held in reference collections (at the WRLFMD or RRL) to determine if any are related (Ferris and Donaldson, 1992). In most cases, antigenic characterisation of the virus will only be available at reference laboratories, so there should be regular submission of representative samples from national FMD laboratories to reference laboratories for this purpose.

Diagnostic tests for specific sample types and approximate time taken to obtain a result from each diagnostic test is outlined in figure 1.

Chapter 2.1.5. of the OIE Manual outlines when different diagnostic tests should be applied, which ones are approved for trade purposes, and details of how to carry out the various tests. In summary, the diagnostic tests available for

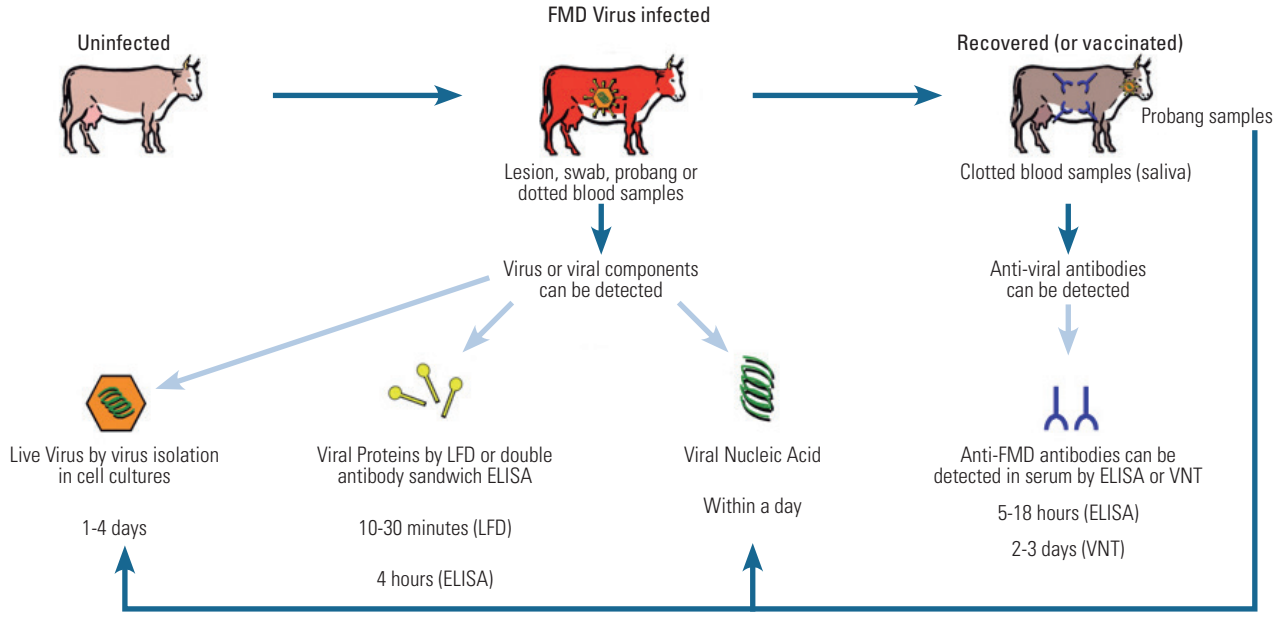

Figure 1: Principles of FMD diagnosis (FAO, date unknown) showing which diagnostic tests can be used on different samples depending on stage of infection/vaccination and the approximate time taken to generate a result from each diagnostic test

identifying the agent FMDV and for identifying an immune response to the agent (antibody detection) are listed in Box 3. Not all of the tests listed will be available at the national level but most will be available at OIE/FAO reference laboratories for FMD.

Box 3: Major diagnostic tests available for FMD

Identification of the agent (FMDV)

- Virus isolation using cell culture
- Antigen capture ELISA (ELISA typing)
- Reverse Transcription (RT) polymerase chain reaction (PCR)
- Real time RT-PCR
- Sequencing
- Lateral flow device (pen-side test)

Serological Tests

- Liquid phase blocking ELISA (LPB-ELISA)
- Solid Phase Competition ELISA
- NSP ELISA (testing for antibodies to viral Non-Structural Proteins (NSP))
- R-value by LP ELISA (used for vaccine-matching)

Sample collection and submission

The quality of laboratory diagnosis depends, amongst other factors, on the selection and quality of samples submitted to the laboratory. Selecting the correct type of sample for the objective of testing and/or for the stage of infection in an individual animal is vital in order to obtain a useful result from laboratory testing. Submission of full epidemiological information on samples submitted is also essential for interpretation of test results (FAO, date unknown). In addition to sample quality, the quantity of samples submitted for laboratory diagnosis and/or for further characterisation of virus must be appropriate for establishing an understanding of FMD epidemiology and FMD risks in a particular geographical location. Low numbers of sample submissions and variable sample quality is a major constraint to understanding epidemiology and risks across many of the SEACFMD Member Countries. Improving the quantity and quality of samples submitted to national laboratories as well as OIE reference laboratories continues to be an area of focus for strengthening regional FMD control.

For further information on sample selection, collection and submission refer to the manual on sample collection and transport and Chapters 1.1.1. and 1.1.2. of the OIE Manual.

The following sections will consider the diagnostic tests and laboratory capacity required for achieving and maintaining OIE recognised FMD free status (with or without vaccination); for achieving OIE endorsement of an official FMD control program; and to achieve different stages of the PCP-FMD.

Laboratory capacity for OIE recognition of FMD free status or endorsement of an official FMD control program

An effective laboratory service is an essential component of any early detection system and is also necessary for countries to fulfil their reporting obligations to OIE on listed animal diseases.

According to the OIE Terrestrial Animal Health Code, a country must be able to provide details of laboratory capacity and details of laboratory based diagnosis as part of an application for OIE recognition of FMD freedom (with or without vaccination) and for OIE endorsement of an official FMD control program. Details of these requirements are outlined in Table 1 (SEACFMD, 2014). Further detail on specific requirements can be found in the relevant sections of the OIE Manual which are also listed in Table 1.

The information presented in Table 1 highlights the need for FMD free countries to maintain sufficient laboratory diagnostic capacity to ensure that any suspected cases of FMD can be rapidly and accurately diagnosed and that the laboratory can cope with sudden increases in demand should an outbreak of FMD occur. Maintaining this level of laboratory capacity should form part of an early detection and response system and details should be provided in emergency preparedness and response plans (see Manual 11). Information in the plan should include, *inter-alia*: details of the maximum (surge) capacity of the laboratory; any arrangements in place for directing samples to other laboratories; and turn-around times for diagnostic test results. Validation of diagnostic test results should be maintained through quality assurance systems and inter-laboratory proficiency testing. Further detail of the actual standards and requirements are outlined in the relevant sections of the OIE Manual and the OIE Terrestrial Animal Health Code.

Details to be reported	Article 1.6.6: Report on FMD Laboratory Diagnosis of a Member Country which applies for recognition of status, under Chapter 8.8. of the Terrestrial Code, as….		Article 1.6.11: Report of a Member Country which applies for the….
	…an FMD free country or zone not practicing vaccination	…an FMD free country or zone practicing vaccination	… OIE endorsement of its official control programme for FMD under Chapter 8.8. of the Terrestrial Code
General information	Provide documentary evidence that the provisions in Chapters 1.1.2., 1.1.3. and 2.1.5. of the Terrestrial Manual are applied	Provide documentary evidence that the provisions in Chapters 1.1.2., 1.1.3. and 2.1.5. of the Terrestrial Manual are applied	Provide documentary evidence that the provisions in Chapters 1.1.2., 1.1.3. and 2.1.5. of the Terrestrial Manual are applied
FMD Laboratory diagnosis in the country	List of approved laboratories OR the name(s) of and the arrangements with the laboratory(ies) samples are sent to, the follow-up procedures and the time frame for obtaining results.	List of approved laboratories OR the name(s) of and the arrangements with the laboratory(ies) samples are sent to, the follow-up procedures and the time frame for obtaining results.	List of approved laboratories OR the name(s) of and the arrangements with the laboratory(ies) samples are sent to, the follow-up procedures and the time frame for obtaining results.
			When applicable, indicate the laboratory(ies) where samples originating from any zone are diagnosed.
			Describe frequency/regularity of submission of samples from the country or zone to a laboratory that carries out diagnosis and further characterisation of strains in accordance with the standards and methods described in the Terrestrial Manual
Approved FMD laboratories in the country	General overview of the FMD approved laboratories	General overview of the FMD approved laboratories	General overview of the FMD approved laboratories
	Procedures for the official accreditation; details of the internal quality management systems	Procedures for the official accreditation; details of the internal quality management systems	Procedures for the official accreditation; details of the internal quality management
	Participation in inter-laboratory validation tests	Participation in inter-laboratory validation tests	Participation in inter-laboratory validation tests

Table 1: Details of FMD laboratory diagnosis required for each specific category for official OIE recognition of status or endorsement by the OIE of an official FMD control program (SEACFMD, 2014).

CASE EXAMPLE: IMPROVED PROFICIENCY TESTING CAPACITY (Vietnam)

Improving laboratory diagnostic capacities of the National Centre for Veterinary Diagnostic (NCVD) and the Regional Animal Health Centre Number 6 (RAHO6)

To improve Proficiency Testing (PT) capacity of Vietnam, two training programmes on were conducted in 2015 as recommended by Reference Laboratory for FMD in South East Asia (RL). The training aimed to strengthen laboratory capacity and ensure implementation of a standardized protocol for FMD diagnosis under an accredited quality assurance system. The two-week training on FMD diagnostics capacity was attended by staff from the National Centre for Veterinary Diagnostic (NCVD) and Regional Animal Health Centre Number 6 (RAHO6) which was held at the Reference Laboratory (RL) in Pakchong, Thailand. The training was focused mainly on practical session on quality assurance. An on-site training was further conducted at NCVD in Hanoi and RAHO6 in Ho Chi Minh City to provide trouble shooting in Proficiency Testing on 8-14 March and 15-20 March, respectively.

Countries seeking OIE endorsement of an official FMD control program should demonstrate that FMD laboratory(ies) in that country have adequate laboratory diagnostic capacity to fulfil their role as part of the control program (including the volume of samples which can be processed, the available tests, quality management systems in place and inter-laboratory proficiency testing). It is also necessary to demonstrate that samples are submitted regularly to national laboratories for diagnosis and to reference laboratories for further characterisation of FMDV. Again, the detail of these requirements should be referred to in the appropriate sections of the OIE Manual and the OIE Terrestrial Animal Health Code.

Laboratory capacity and the progressive control pathway for FMD

Although some SEACFMD Member Countries have achieved OIE free status for FMD and others have had official FMD control programs endorsed by OIE, many of the SEACFMD Member Countries remain endemic for FMD and are at an earlier stage in the process of understanding and controlling the disease within their country. The PCP-FMD is a system which, following appropriate consultation, has become a joint FAO/OIE tool and forms a key component of the Global FMD Control Strategy. The purpose of the PCP-FMD is to assist and facilitate countries to progressively reduce the impact of FMD and the load of FMD virus (FAO, OIE and EUFMD, 2011) and thus move towards controlling and eradicating the disease in a step-wise manner.

The PCP-FMD consists of stages which outline different FMD control activities (see Figure 2) and is based on developing an understanding of the epidemiology of FMD and then applying targeted, risk-based control strategies in order to control the disease in key areas. By implementing these activities at the different stages, countries should progressively increase the level of FMD control to the point where an application for OIE endorsement of a national FMD control program or official freedom from FMD with or without vaccination (end of stages 4 or 5, respectively) may be successful and the status sustainable (FAO, OIE and EUFMD, 2011).

Veterinary laboratories will play a vital role in supporting the different activities conducted under the PCP-FMD including: testing serological samples generated through active surveillance studies; confirming diagnosis of clinical or suspect cases; post-vaccination monitoring; and/or substantiating freedom from infection in specific populations. Throughout the PCP-FMD, laboratory diagnostic capacity should evolve to reflect different roles as the country progresses through the stages in the pathway towards eradication of FMD. Indeed, laboratory capability is one of the key requirements for stage progression through the PCP-FMD (Box 4).

Box 4: Progressive Control Pathway for FMD: Requirements for Progression
(Paton (date unknown))

- Political and social participation
- Regional integration
- Knowledge of livestock production systems
- Effective Veterinary Services
- Disease surveillance
- Diagnostic capability
- Vaccination
- Emergency response

The information contained in the current section of this manual is largely based on a document developed by FAO and EUFMD entitled: Guidelines for the assessment of laboratory capacity to undertake diagnostic services in the framework of the PCP-FMD stages 1-3 (FAO and EUFMD (date unknown)), hereafter referred to as the FAO EuFMD Laboratory Assessment Guidelines. Readers should refer to this document for further information on this subject.

The descriptions provided in Box 5 outline the necessary laboratory diagnostic capacity/laboratory services for national FMD laboratories at different stages of the PCP-FMD, including capacity to collect and submit samples to reference laboratories. The diagnostic services required at each stage reflects the objectives of diagnostic testing at each of the different PCP stages.

Table 2 provides further detail of which diagnostic assays for FMD should be available for different stages of the PCP-FMD, together with the rationale for using the different assays. For further detail on these, and other diagnostic tests for FMD, refer to the OIE Manual and FAO EuFMD Laboratory Assessment Guidelines. (date unknown). The SEACFMD manual on Sample Collection and Transport also provides further information on use of diagnostic assays.

FMD Reference Laboratories

OIE Reference Laboratories are designated to pursue all the scientific and technical problems relating to a named disease

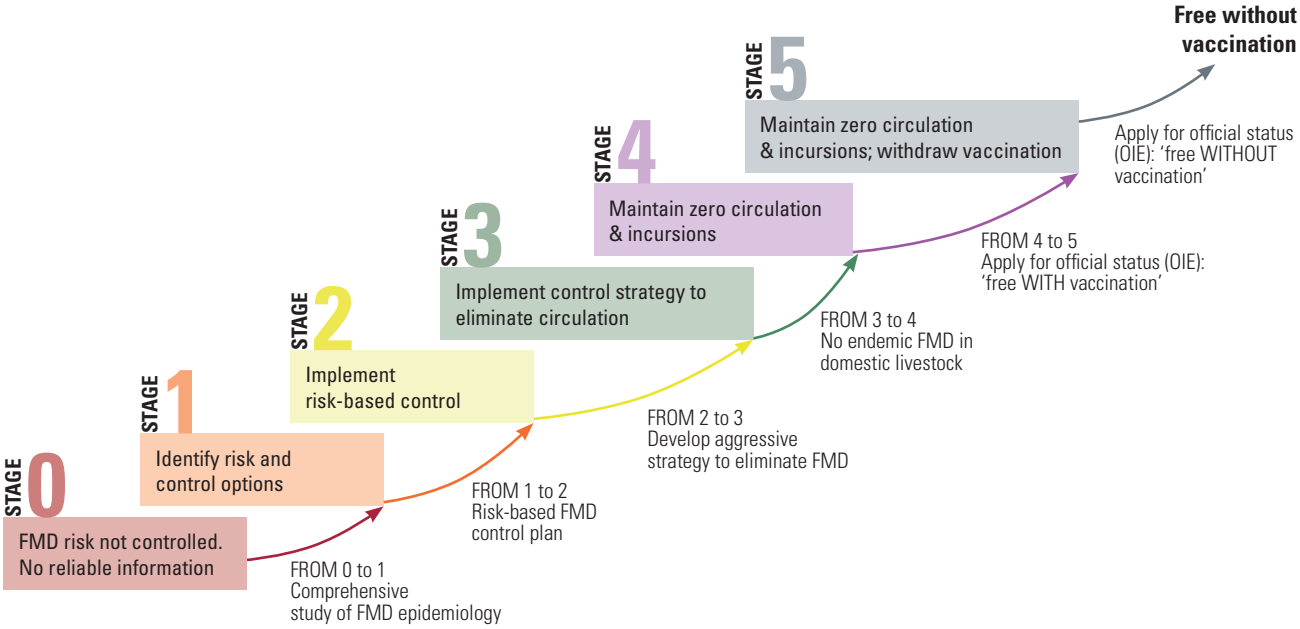

Figure 2: Stage progression in the progressive control pathway (FAO, OIE and EUFMD, 2011)

Box 5: Necessary diagnostic services for stages 1-3 of the Progressive control pathway for foot and mouth disease

(FAO and EUFMD (date unknown))

PCP stage 1 laboratory services

PCP stage 1 description: identify risk and control options

At this stage it is important that the laboratory can guarantee the following services:

- Carry out ELISA testing for NSP antibody detection
- Test tissue samples through ELISA for a preliminary identification of serotypes
- Ship samples on a regular basis to an international reference laboratory

PCP stage 2 laboratory services

PCP stage 2 description: Implement risk-based control

In addition to the basic services provided in stage 1, laboratory tests are needed in stage 2, to measure and monitor the effects of control programs (Structural Protein antibody tests for post-vaccination monitoring and Non-Structural Protein antibody tests for measuring incidence and prevalence of FMD infection). For this stage the introduction of RT-PCR should be considered. It is, in fact, likely that the monitoring program to be implemented in the subgroups targeted by control measures (most likely vaccination) will be based also on detection of viral genome in non-clinically affected animals.

PCP stage 3 laboratory services

PCP stage 3 description: Implement control strategy to eliminate circulation

In stage 3 of the PCP-FMD, the emphasis is on earliest detection of infection and on demonstrating limited spread in time and space. Therefore, RT-PCR testing and high throughput NSP testing should be operational. Also strain characterisation (shipping samples to RRL and WRL) is important for demonstrating that FMD incursions are exotic. Furthermore, laboratory diagnostic capacity should be at least the same as for stage 2.

on the OIE list (OIE, 2016a). There are a number of FMD reference laboratories distributed throughout the world and operating at national, regional and global levels (see section on laboratory networks). A list of OIE designated FMD reference laboratories can be found at the following link:

http://www.oie.int/our-scientific-expertise/reference-laboratories/list-of-laboratories/

A reference laboratory represents a center of excellence for a particular disease in that it generally has access to experts knowledgeable about the disease and the control of that disease, together with others who have specialist skills in the diagnostic methods appropriate for the disease (Edwards and Alexander, 1998). OIE reference laboratories provide scientific and technical assistance, advice and capacity building for OIE Member Laboratories. They may also

PCP stage	Assay	Purpose	Level of discrimination	Necessary/ desirable/neutral
1-2	Antigen capture ELISA	Identification of the agent (Diagnosis/Surveillance)	Type-specific	Necessary
1-2	Lateral flow device	Identification of the agent (Diagnosis/Surveillance)	General	Desirable
1-3	NSP ELISA	Serology (Surveillance)	General	Necessary
1-3	Submission of samples for vaccine matching/sequencing to RRL/WRL	Strain characterisation	Subtype/strain specific	Necessary
2	Solid-phase competition ELISA	Serology (Surveillance)	Serotype-specific	Desirable (post vaccination monitoring)
2	Liquid Phase Blocking ELISA (LPB ELISA) for structural antibodies	Serology (Surveillance)	Serotype-specific	Desirable (post vaccination monitoring)
2-3	(real-time) RT-PCR	Identification of the agent (Diagnosis/Surveillance)	General	Desirable (stage 2) Necessary (stage 3)
2-3	(real-time) RT-PCR	Identification of the agent (Diagnosis/Surveillance)	Serotype-specific	Desirable (2) Necessary (3)
2-3	Virus isolation	Identification of the agent (Diagnosis)	General	Neutral
2-3	Virus Neutralisation Test (VNT)	Serology (Surveillance)	Type-specific	Neutral (post vaccination monitoring)
2-3	LPB ELISA	Serology (Surveillance)	Type-specific	Necessary (post vaccination monitoring)
3	NSP ELISA	Serology (Surveillance)	General	Necessary (High throughput surveillance)

Table 2: Assays for FMD virus and antibody detection in relation to PCP stages 1-3 (adapted from FAO and EUFMD (date unknown))

coordinate scientific and technical studies in collaboration with other laboratories or organisations (OIE, 2010).

In order for reference laboratories to fulfil their role on behalf of the international community, it is essential that OIE member countries support OIE Reference Laboratories through submission of specimens, isolates of infectious agents and other information of potential regional or international significance (based on information from Chapter 1.1.0. of the OIE Manual).

World Reference Laboratory

The Pirbright Institute in the U.K. was designated as the World Reference Laboratory (WRL) for Foot-and-Mouth Disease by FAO in 1958 (Ferris and Donaldson, 1992) and later as a reference laboratory for FMD by the OIE. The WRLFMD initially represented the only reference laboratory for FMD but has since become the leading laboratory amongst a global network of reference laboratories.

In addition to the samples tested and viral isolates characterised at the WRL, this is also the centre where information about viruses are collated in order to analyse the distribution and movement of different FMD viral strains globally and to provide information relating to this data to other OIE Member Countries. The WRLFMD also has capability to conduct full-genome sequencing which allows high resolution tracing of FMD spread to the level of farm to farm transmission. Although these roles have been highlighted, WRLFMD provides many more services to OIE member countries and is involved in research relevant to FMD and development of diagnostic tests, vaccines, etc.

For more information on the WRLFMD, including the services offered and details about sample submission, visit the WRLFMD website: http://www.wrlfmd.org/

Regional Reference Laboratories

The following description provides information about the two OIE-designated Regional Reference Laboratories in South-East Asia and China: RRL-Pakchong in Thailand and RRL-Lanzhou in China. The achievements of these laboratories in gaining recognition as OIE reference laboratories and the work undertaken at these laboratories provides vital support to the SEACFMD campaign and will continue to play a key role in the SEACFMD strategic plan for FMD control.

RRL Pakchong

RRL-Pakchong is a key laboratory in the SEACFMD Laboratory Network (LabNet). The RRL opened in 2004 and was designated by the OIE as a reference laboratory for FMD in 2010 and, as such, it is now a member of the OIE/FAO FMD reference laboratory network.

RRL Pakchong provides a number of services and takes part in activities with other OIE reference laboratories and also with non-OIE reference laboratories from other OIE member countries (particularly in South-East Asia). The following list is an example of the activities conducted by RRL Pakchong (based on information from Kamolsiripichaiporn, 2014):

- Perform diagnostic tests for FMD for the purposes of disease diagnosis, screening animals for export, surveillance, etc. (both for Thailand and for other OIE member countries)
- Supply standard reference reagents to laboratories in other OIE Member Countries
- Development of new diagnostic methods validated according to OIE standards
- Provision of expert advice
- Participate in international scientific studies with other OIE Member Countries
- Collection of epizootiological data relevant to international disease control
- Dissemination of epizootiological data that has been processed and analysed
- Provision of scientific and technical training to laboratory personnel from other OIE Member Countries
- Organisation of/participation in scientific meetings on behalf of OIE
- Exchange information with other OIE FMD reference laboratories
- Involvement in maintaining a network with OIE FMD reference laboratories by participating in proficiency tests
- Collaboration with other FMD reference laboratories on scientific research projects for the diagnosis or control of FMD
- Organise inter-laboratory proficiency testing with laboratories other than OIE reference laboratories (SEACFMD Member Countries)
- Place expert consultants at the disposal of OIE

As described earlier in this manual, OIE reference laboratories depend upon the submission of adequate quantity and quality of samples from the field in order to fulfil their purpose. It is the responsibility of SEACFMD member countries to ensure that a sufficient number and quality of samples are submitted to national laboratories and also regular submissions made to reference laboratories. See manual on sample collection and transport for further information.

RRL Lanzhou

Lanzhou Veterinary Research Institute (LVRI) was designated as an OIE reference laboratory for FMD in 2011. This laboratory provides services to other OIE member countries in addition to supporting the FMD control program in China. The activities conducted at RRL Lanzhou are, in general terms, similar to those of other reference laboratories. RRL Lanzhou also has active research and development activities focusing on development of new diagnostic tests and vaccines for FMD. Further details about RRL Lanzhou can be found at: http://www.chvst.com/English_web/list.aspx?id=3240

Laboratory networks

Laboratory networks for FMD function at a number of different levels. There is a global OIE/FAO FMD reference laboratory network which is made up of key national and regional reference laboratories (figure 3) and is led by the WRLFMD, Pirbright.

The SEACFMD Member Countries also have an active regional FMD laboratory network (LabNet) which includes RRL-Pakchong in Thailand, RRL-Lanzhou in China and national FMD laboratories from the other SEACFMD Member Countries.

According to Paton (date unknown), international laboratory networking contributes the following benefits to FMD on a global and/or regional level:

- Sharing best practice and raising standards
  - Building up capability in support of regional control programs.
  - Developing trust and shared vision through ongoing contact and joint programs of work (transparency).
- Global (or regional) risk awareness and early warning
  - Accurate and timely global surveillance information.
  - Vaccine bank reference for FMD free countries.

Strengthened communication and transparency on a regional and global level benefits control of FMD and, through sharing experience and expertise including inter-laboratory proficiency testing conducted amongst laboratory networks, overall laboratory diagnostic capacity should be strengthened. With improved communication between laboratories will come greater confidence in results generated from member country laboratories. This could carry significant benefits to facilitating trade agreements between countries in the region, where diagnostic testing is used as part of the certification process for traded livestock and livestock product.

Laboratory networking also helps to share expertise through shared training and/or exchange programs where personnel from one laboratory can spend time in another laboratory within the network to build skills in a particular area. This may also be useful for maintaining expertise in personnel from FMD free countries who may have limited opportunity to run FMD diagnostics in their own country and can maintain skills through visiting laboratories in countries where FMD is endemic.

The Global OIE/FAO FMD Reference Laboratory Network

This laboratory network includes all FAO and OIE FMD reference laboratories across the globe (Figure 3) and is a vital contributor to the global control of FMD and provides opportunities and expertise for developing and sustaining laboratory capacity and capability, exchange of materials and technologies, harmonising approaches to diagnosis and supporting complementary research (Hammond, 2012).

Laboratories within the network regularly receive samples for FMD diagnosis from many parts of the world and, through characterisation of viruses (partial or full-genome sequencing), they are able to trace the origin of viruses by comparing them with other viruses held in collections (Hammond, 2012). In this way, a global picture of the distribution and spread of FMD virus strains can be established thus providing valuable information on FMD epidemiology as well as functioning as an early warning system. Again, the value of this system depends upon the timely submission of sufficient quality and quantity of samples, accompanied by detailed epidemiological information.

Another key role of the reference laboratories within the network is vaccine matching and advising countries on suitable vaccine strains for viruses against which specific populations of livestock need protection.

SEACFMD Laboratory Network

Active laboratory and epidemiology networks are an important component of a regional FMD control strategy, as outlined in the OIE/FAO Global FMD Control Strategy.

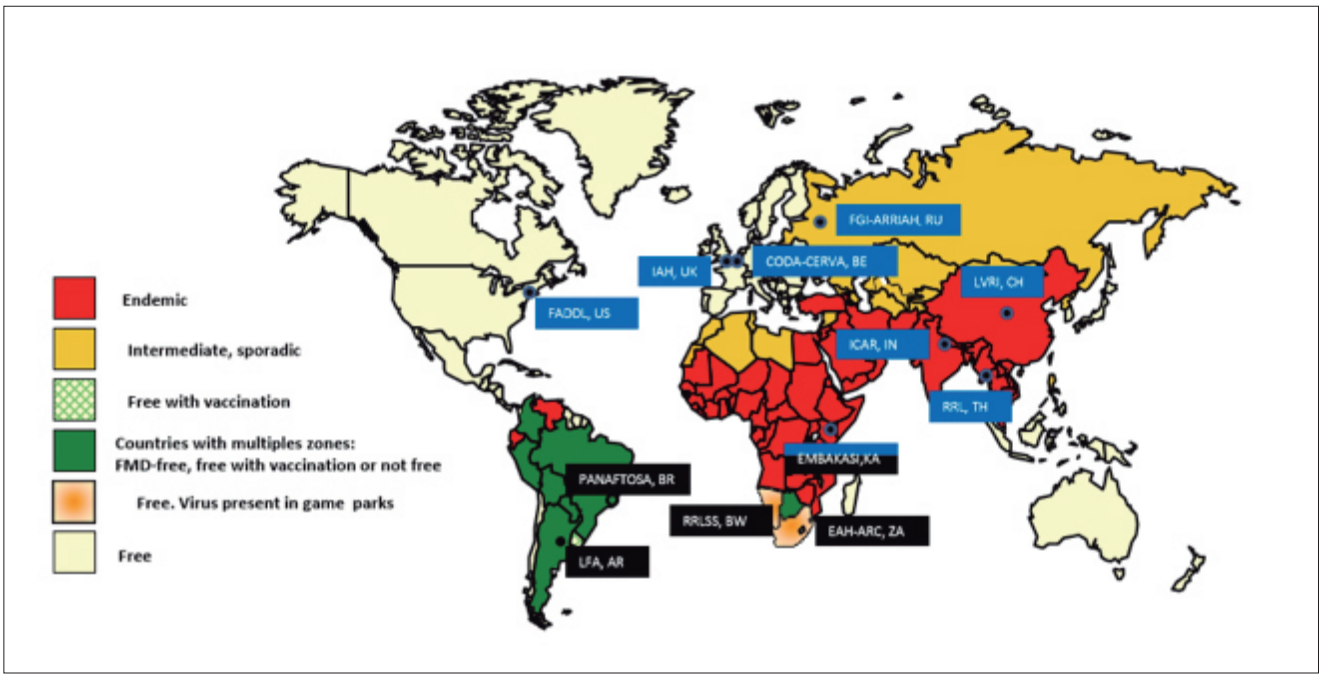

Figure 3: OIE/FAO foot and mouth disease laboratories network (Paton (date unknown))

The SEACFMD Laboratory Network (LabNet) comprises representatives of national laboratories from each of the SEACFMD Member Countries (including those which are FMD free) together with two OIE accredited regional reference laboratories for FMD: RRL-Pakchong in Thailand and RRL-Lanzhou in China. Experts and researchers, such as those from partner laboratories in other countries including Australia, the Republic of Korea, Japan and China are also invited to attend. The SEACFMD LabNet meets on an annual basis, often with the SEACFMD epidemiological network (EpiNet), but maintains communications through the network at other times.

The SEACFMD LabNet plays a pivotal role in the regional FMD control strategy for South-East Asia and China. Existence of a regional laboratory network enhances rapid diagnosis of FMD viruses through early detection and confirmation of FMDV serotypes. Sharing of this information amongst members of the network improves the regional early warning system and transparency between SEACFMD Member Countries. Virus characterisation and vaccine matching at regional reference laboratories and sharing this information amongst LabNet members helps to ensure availability and selection of suitable vaccines. The SEACFMD LabNet also facilitates sending of field isolates from national FMD laboratories in South-East Asia to RRL for confirmatory diagnosis, further characterisation, and/or vaccine matching. Increased numbers of samples available at reference laboratories for molecular epidemiology helps to improve surveillance through mapping evolution and spread of FMDV serotypes (and sub-types). The linkage between SEACFMD LabNet and EpiNet is important for optimising regional surveillance, diagnostic and control activities, and so communication within and between the two networks should be maintained throughout Phase 5 of the SEACFMD Campaign.

The SEACFMD LabNet also takes part in inter-laboratory proficiency testing, led by RRL-Pakchong, in order to strengthen capacity of national laboratories through arrangement of personnel training and/or exchange between laboratories to improve skills in specific areas (see section on FMD reference laboratories). Training, and skill maintenance, in diagnostic capacity, QA and OH&S remains an important ongoing requirement throughout the SEACFMD Campaign.

Laboratory twinning

Laboratory twinning is a concept adopted by the OIE with the aim of creating more OIE reference laboratories and collaborating centres in geographic areas previously under-represented and to achieve a better balance in the global distribution of high level laboratory expertise (OIE, 2010). The twinning concept involves pairing an existing OIE reference laboratory with a candidate laboratory. Within this arrangement the reference laboratory provides the candidate laboratory with technical support, guidance and training such that the candidate laboratory is brought closer to OIE reference laboratory status through improving standards in specific areas (OIE, 2010).

Most twinning projects last between one and three years. For further details on laboratory twinning, including details of submitting a proposal for twinning projects, refer to OIE (2010).

OIE PVS Tool

The OIE Tool for the Evaluation of Performance of Veterinary Services (OIE PVS Tool) represents a key way in which veterinary laboratory capacity can be evaluated in OIE Member Countries, alongside evaluation of other aspects of Veterinary Services (Figure 4).

The OIE PVS Tool is designed to assist Veterinary Services to establish their current level of performance, to identify gaps and weaknesses in their ability to comply with OIE international standards, to form a shared vision with stakeholders (including the private sector) and to establish priorities and carry out strategic initiatives (OIE, 2016b). The 'PVS laboratory tool' is a method of assessing the national veterinary laboratory network to determine whether, and to what extent, the national laboratory infrastructure meets the needs of the Veterinary Services, is sustainable and is regularly audited (OIE, 2014).

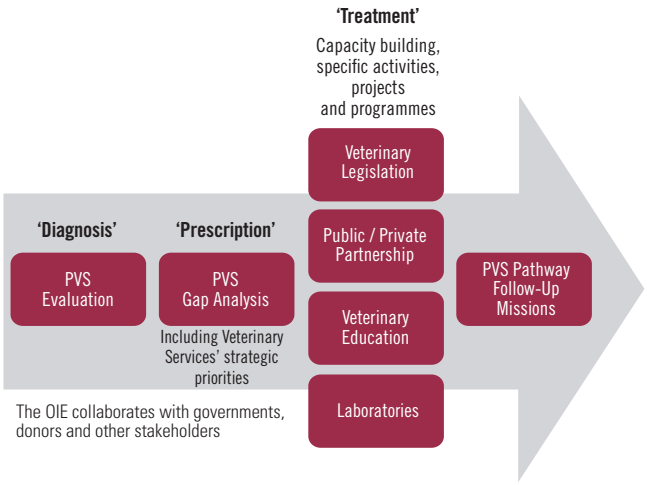

Figure 4: OIE PVS Pathway (OIE, 2016b)

A PVS laboratory mission is conducted upon request of the country by veterinary laboratory specialists after the initial PVS evaluation and PVS gap analysis have been completed. This mission determines to what extent the national laboratory network meets the needs of the Veterinary Services and identifies priority areas for capacity building.

For further information on the PVS pathway and PVS laboratory tool, refer to the following references: OIE, 2013; OIE, 2014; OIE, 2016b.

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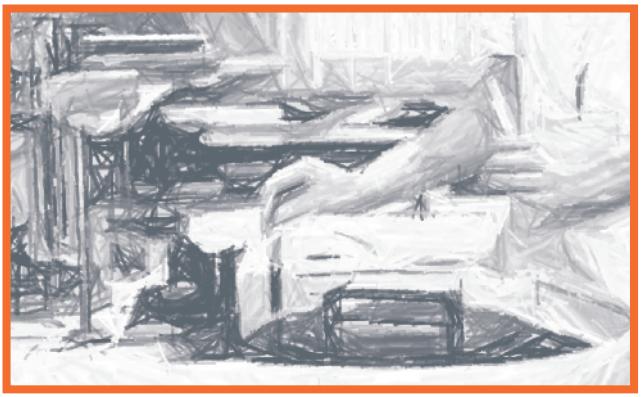
Manual 8

Laboratory support



World Organisation for Animal Health
12, rue de Prony
75017 Paris, France
Tel.: 33-(0)1 44 15 18 88
Fax: 33-(0)1 42 67 09 87

www.oie.int

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