

MINIMUM STANDARDS FOR LABORATORIES WORKING WITH FOOT-AND-MOUTH DISEASE VIRUS *in vitro* AND *in vivo*
What have we learned from the FVO Inspections?
Bernd Haas, FLI Riems, Germany



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MINIMUM STANDARDS FOR LABORATORIES WORKING WITH FOOT-AND-MOUTH DISEASE VIRUS *in vitro* AND *in vivo*
Conclusions:

The „Minimum Standards“ proved to be a valuable tool for the management of laboratory bio-risks and the FVO inspections.

The 2009 revision improved the „Minimum Standards“ significantly. However, it contains some ambiguities and duplications.

Several member states maintain national laboratories able to diagnose FMD in case of an outbreak which are **important for the whole European Community**.

However, they **lack the funding** for a facility fully complying with the „Minimum Standards“. A standard for diagnostic labs which don't amplify virus nor use live FMDV as reagents is needed.

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Recommendations:

- Update Council Directive 2003/85/EC in respect to “auxiliary labs”
- Update “Minimum Standards” in respect to “auxiliary labs” and to remove some duplications and ambiguities
- Create an expert committee on lab bio-risk management to support the Commission as well as national competent authorities
- Allocate sufficient funding for diagnostic and research laboratories

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History **Loeffler’s animal facility: „High containment“ anno 1900**



„...Germany could be considered free of FMD if there weren't Prof. Loeffler's experiments...“

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History **FLI 1990** **1950th - present: „High Security buildings“**



- Constant **negative pressure**
- **Double HEPA filters** (exhaust)
- **Automatic flaps** (inlet and exhaust)
- **Thermal decontamination of waste water** (within containment)
- **Chemical decontamination of equipment**
- **Compulsory Shower-Out**
- **Animal Carcass Rendering**
- **Emergency Power Supply**

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History

Diagnostic Tests **Containment Standards**
 UK, Dk, Ge, Nl, It, CH...
 MINIMUM STANDARDS 1985/93 MINIMUM STANDARDS 2009

high risk
 low risk
 1910 2001 2010 timeline

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History



COMMISSION WORKING DOCUMENT
for adoption at
the 38th General Session
of the European Commission
for the Control of FMD (EuFMD) - April 2009

**MINIMUM STANDARDS FOR LABORATORIES WORKING WITH
FOOT-AND-MOUTH DISEASE VIRUS *in vitro* AND *in vivo***

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History

Specific Requirements

Management

Training

Laboratory Biosecurity

Personnel (limit access, shower, quarantine...)

Facility Design

Handling of FMD virus

Airhandling systems (negative pressure, HEPA...)

Waste and effluent treatment

Removal of equipment, Removal of biological material

Decommissioning

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What was new in 2009?

Terminology used and the **biorisk management principles** incorporated adapted from the Draft CEN/CWA "Laboratory Biorisk Management Standard"

- Bio-risk policy
- Responsibilities and independence of BRO
- Continual improvement process
- Risk/threat assessment
- Accident and incident reporting system
- Emergency procedures
-

Almost **no changes** in respect to "**hardware**" and buildings

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What was new in 2009?

Biorisk
combination of the **likelihood** of the occurrence of an **adverse event** involving exposure to biological agents and toxins and the **consequence** (in terms of accidental infection, toxicity or allergy or unauthorised access, loss, theft, misuse, diversion or release of biological agents or VBMs) of such an exposure.

Biorisk officer (BRO) or biorisk advisor (Biosafety / Biosecurity Officer) a staff member of an institution who has **expertise** in the biohazards encountered in the organisation and is competent to **advise** top management and staff on biorisk management issues

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What was new in 2009?

Biosafety
Laboratory biosafety describes the containment principles, technologies and practices that are implemented to prevent the **unintentional** exposure to biological agents and toxins, or their accidental release.

Biosecurity
Laboratory biosecurity describes the protection, control and accountability for valuable biological materials within laboratories, in order to prevent their loss, theft, misuse, diversion of, unauthorised access, or **intentional** release.

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What was new in 2009?

Primary containment layer:
contains the live FMDV at source within closed containers or a class I, II or III microbiological safety cabinet, or in the case of infected animals, contains the live FMDV by physical containment in specially constructed rooms with treatment of all waste and the HEPA filtration of air

Secondary containment layer:
contains FMDV of infected materials and staff working with such materials within a closed and highly controlled physical environment and subject solids, fluids and air to a treatment by validated procedures that will remove or inactivate FMDV

Tertiary containment layer:
prevents contact between the live FMDV and susceptible livestock outside containment by appropriate measures, such as restrictions placed on access of staff to such livestock.

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What was new in 2009?

Risk-Analysis

The main sources of FMDV are:

- infected pigs, cattle, sheep, goats and other susceptible **large animals**
- laboratory based physical and chemical processing of large quantities of virus
- infected laboratory animals, e.g. baby mice and guinea pigs
- infected tissue cultures
- diagnostic specimens**

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Authorization of laboratories in respect to FMD

1. infection of experimental and/or large **animals** with FMDV; **„Real FMDV lab“**
2. activities which produce high amounts of infectious FMDV, e.g. large scale virus production at a capacity that involves **more than 10 litres** of cell culture
3. activities involving the handling, and in particular, the propagation of infectious FMDV, but are **limited to 10 litres** of cell culture, and during which the FMDV is enclosed in containers which can be effectively autoclaved or disinfected;
4. test diagnostic samples for antibody to FMDV, by methods that do not involve live FMDV manipulation; **„Auxiliary FMD lab“**
5. test diagnostic samples for FMDV genome by methods that do not involve live FMDV manipulation (e.g. RT-PCR);
6. apply on the genome of FMDV methods of molecular biology that do not involve live FMDV manipulation **usually: „normal lab“**

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What was new in 2009?

Annex: Standard for Auxiliary Diagnostic Labs for Emergencies

MINIMUM STANDARDS OF BIORISK MANAGEMENT FOR LABORATORIES UNDERTAKING DIAGNOSTIC INVESTIGATIONS OF LOW-RISK SAMPLES DURING AN OUTBREAK OF FMD

relates to the use of laboratory tests which do not contain or require live FMD virus

- for the testing of blood samples from holdings without clinical signs
- any samples from any holding that have been treated in a way that ensures the inactivation of FMDV infectivity

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FVO-INSPECTIONS OF FMD FACILITIES

2009-2012

In accordance with Article 66 of **Directive 2003/85 EC**, the FVO has inspected all **15 laboratories** and **3 vaccine plants** handling infectious FMDV and listed in Annex XI of the Directive.

Results on specific laboratories are strictly confidential!

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FVO Inspections

The inspections were carried out by the **Food and Veterinary Office (FVO)** on the legal basis of Council Directive 2003/85/EC during 2010 - 2012.

The inspection teams were comprised of **one FVO inspector** and **two experts** from European FMD laboratories with considerable experience in FMD work and bio-risk management.

The **“Minimum Standards”** were used as the technical basis for the inspection of laboratories and vaccine plants handling infectious FMDV.

After completion of the first round of inspections, it’s time for a **critical review** of the FMD risk management practises in Europe and a revision of the Minimum Standards.

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FVO Inspections - Legal Aspects

Article 65 of Council Directive 2003/85/EC requires the Member States (MS) to ensure that:

- (a) laboratories and establishments, in which live foot-and-mouth disease virus, its genome, antigens or vaccines produced from such antigens are handled for research, diagnosis or manufacture, are strictly **controlled** by the **competent authorities**;
- (b) the handling of live foot-and-mouth disease virus for research and diagnosis is carried out only in **approved laboratories** listed in Part A of Annex XI;
- (c) the handling of live foot-and-mouth disease virus for the manufacturing of either inactivated antigens for the production of vaccines or vaccines and research, is carried out only in the **approved establishment** and laboratories listed in Part B of the Annex XI.

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FVO Inspections - Legal Aspects

(d) the laboratories and establishments referred to in points (b) and (c) are operated at least according to the

biosecurity standards set out in Annex XII. = „Minimum Standards“

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FVO Inspections - Findings

Transposition of law
 Article 65 of Council Directive 2003/85/EC has not been fully transposed into the national legislation.

Designation of the competent authority (CA)
 Often unclear, ministry or local or regional authority without specific knowledge on bio-risk management

Approval of the laboratory to handle live FMD virus
 Often no specific approval for FMD work

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FVO Inspections - Findings

Organization of official controls
 Often no structured approach
 In most facilities controls were not carried out or did not sufficiently cover FMD bio-risk management

If there was good bio-risk management, it was due to an internal structure of the lab!

Enforcement powers
 Usually in place

Notification procedures in case of emergencies
 Often on an ad hoc basis

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FVO Inspections - Findings

Qualification of the CA inspectors
 Entirely inadequate to inspect complex bio- risk management systems, in particular the technical installations of the air ventilation systems and the effluent treatment plants

Inspectors usually come from local or regional authority without specific knowledge on bio-risk management

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FVO Inspections - Findings

In several facilities:

Labs sometimes more or less OK

but

Conditions of HEPA filters unknown, no measurements, no knowledge

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FVO Inspections - Findings

In several facilities:

Labs sometimes more or less OK

but

Effluent treatment plants in poor conditions, not in containment

Situation sometimes made worse by a shunt between lab sinks and municipal sewage system „in case the plant doesn't work“(1), with a control lever found unlooked and at the outer wall

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FVO Inspections - Findings

In several facilities:

Scientists with (some) bio-risk responsibilities

VS

Staff running effluent and air-handling plants and autoclaves

Sometimes made worse by outsourcing!

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FVO Inspections - Findings

In several facilities:

Nice records on lab floor

VS

Reality downstairs

A senior staff member (BRO) should have felt responsible for the bio-risk aspects of the whole FMD facility

- actually gone downstairs into the cellar and into the attic,
- checked the plants, filter, tubes...
- checked the autoclaves,
- discussed with the craftsmen

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FVO Inspections - Findings

In several facilities:

Nobody had ever asked

- What can go wrong?
- What could result from such a failure?
- How long would it take until you realise something has gone wrong?
Bad: FVO Inspektors find live animals in your effluent treatment tank
Worse: FMD outbreak reported on TV
- What can be done do to control the risk?
e.g. plant in secondary containment, several valves in series, with pressure testing

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FVO Inspections - Findings

In several facilities:

Flimsy „Secondary Containment“

Primary containment Primary containment Primary containment

Problem: Unacceptable for large animal infections and vaccine production
Relies heavily on procedures and on discipline of staff

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FVO Inspections - Findings

Murphy's Law and the importance of a sturdy Secondary Containment

Primary containment Primary containment Primary containment

Problem: Such a type of secondary containment is very expensive; few member states can afford it! Do they all need one for lab diagnosis?

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Suggested improvements

Competent authorities (CA)

Delegate/support technical part of inspections by CAs to an expert group at European level

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Suggested improvements

Laboratories/Facilities

Send BRO to major FMD labs for training!

Allocate sufficient funds for containment!

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Suggested improvements

EuFMD / DG SANCO

Modify "Minimum Standards" according to risk:

"Real" FMD labs doing research and diagnostic work on foreign samples which contain or may contain **live FMDV "in peace times"**

vs

"Auxiliary" labs investigating only **suspect samples** from own country without using live FMDV as a reagent

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Suggested improvements

EuFMD / DG SANCO

Consult

- EuFMD Committee on Research
- FMD laboratory Bio-Risk Officers (BRO)
- Head Engineers of major FMD Laboratories

Consider:

"EU/EuFMD Committee on Lab Bio-risk Management"

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