


Towards a reinforced role for bio-containment manufacturing laboratories

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Introduction



For more than 50 years, bio-containment industrial facilities have manufactured vaccines which greatly help to control and even eradicate foot-and-mouth disease (FMD) in many countries.

These facilities have also proved to be adaptable for the production of vaccines against other emerging diseases such as African horse sickness or bluetongue.



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Bio-security has always been a concern




Many improvements (including bio-containment, use of aziridines for inactivation, and operating procedures) have considerably helped to reach high standards over the years.

Duplicating barriers to virus escape, such as double HEPA filtration, has also been implemented to reinforce the overall efficacy of the bio-security mechanisms.




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A regulatory framework has been defined




- Guidelines for bio-security measures in FMD laboratories were formulated by the EUFMD Commission in 1993 (European Commission for the Control of Foot-and-Mouth Disease, 1993)
- A list of the laboratories and vaccine manufacturers authorized to manipulate FMD virus in the EU is annexed to Directive N° 2003/85EC.
- The 2004 Edition of the *OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* indicates that FMD for diagnostic and vaccine production purposes) should be handled under P3 bio-containment standards




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Why are bio-containment facilities still needed for vaccine manufacture?




- Manufacturers currently use whole-virus inactivated polyvalent vaccine technology, because complete and solid protection is conferred only by vaccines that trigger a large range of immune mechanisms.
- No synthetic or biotechnology-derived FMD vaccine developed to date has been able to surpass consistently the performance of conventional inactivated whole virus vaccines.




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Is there a short term alternative to bio-containment facilities for vaccine manufacture?



- High level of containment (P3 or BSL3+ depending on nomenclatures) is currently required for conventional vaccine manufacture.
- Other FMD vaccine production platforms might be considered, based on the determination of virulence factors of FMDV and the attenuation of FMDV production strains (reverse genetics approach?), to improve even further the bio-security of vaccine production. This is a 5-year research program according to the FMD Roadmap.



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Why are FMD vaccines still needed?

- FMD vaccines help to alleviate the disease burden born by small scale and subsistence farmers of the developing world, for whom FMD often signifies loss of productivity, food scarcity and poverty
- Removing FMD as a livestock scourge from the developing world would not only be of immense benefit in those parts of the world, but would also be a vital step towards removing the risk of FMD permanently from the developed world

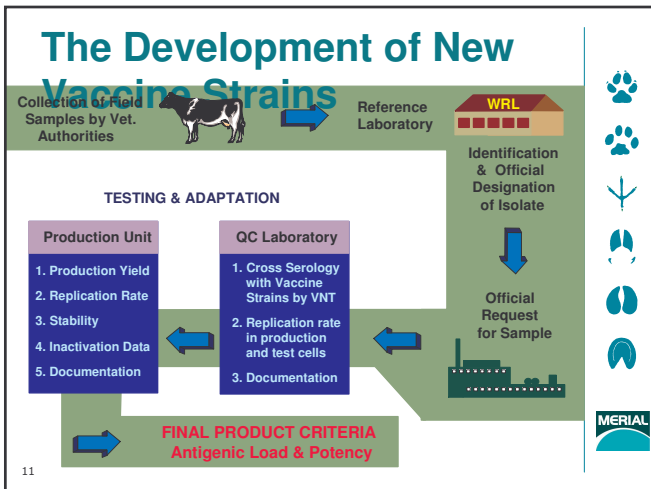
Why are FMD vaccines still needed?

(continued)

Vaccination is today recognized as an essential, highly efficacious and cost beneficial component of FMD prevention and control, provided vaccines are sufficiently effective (through both high potency and adequate strain composition).

Assuring adequate strain composition

- The rapid spread and constant circulation of the virus in indigenous livestock populations and wildlife of the developing world periodically gives rise to new strains of FMD. These evade immunity induced by natural infection or vaccination.
- To assure successful protection, in spite of the antigenic heterogeneity of FMD virus circulating in the field, Merial continuously monitors, screens and regularly develops new vaccine strains found in individual countries or outbreaks.



Why are FMD vaccines still needed?

(continued)

- FMD vaccines protect animals from clinical disease, rare breeds from extinction, and ensure food supply.
- Where disease occurrence is too widespread, vaccination is less disruptive and costly than dealing with outbreaks by bio-security measures only, as they often imply stamping-out which is less and less acceptable to the public

In emergency situations, time is of the essence

- Should the disease spread, emergency vaccination may be practised as an adjunct to the control and eradication measures.
- Emergency vaccination relies on rapid availability of highly potent, antigenically appropriate, safe vaccines, capable of inducing early protection with a single dose and dramatically reducing virus replication in vaccinated livestock when exposed to infection.



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Advantages of Antigen Banks



- Merial has established antigen banks for most FMD-free countries around the world and can supply highly concentrated, NSP-free emergency vaccines at short notice
- The concentrated antigens are stored over liquid nitrogen where they remain stable for at least 5 years.



FMD outbreak: Antigen Bank Emergency response



- Order from the customer for 2.5 million doses of trivalent FMD vaccine
- Implementation of the action plan = order + preparation
- Antigen de-stocking
- Thawing / Blending
- Filling
- Labeling / Packing / Early release
- Vaccines ready to be shipped



Delivery within less than a week: immediate start of the vaccination helps control outbreak



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The FMD threat is increasing

- Globalization of trading activities and population movements make all reservoirs of FMD a potential danger for disease-free countries.
- Large-scale animal movements create a special hazard regarding the spread of FMD
- This will be further exasperated as emerging economies with weaker veterinary services capabilities take a more prominent role in global exchanges
- FMD remains close to the borders of Europe and regularly makes incursions into the European Union



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Why even more vaccines are needed

Vaccines are playing an increasingly important part in global FMD eradication.

It will require more than the combined output of all existing vaccine producers to provide adequate supply in the future.



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Other exotic infectious diseases also have to be considered

- Many human diseases originate from animals and diseases can now spread faster around the world
- The most cost efficient, safe and environmentally acceptable way to deal with these diseases is through rigorous prevention and control.
- Preparedness on all levels of the Veterinary Public Health sector is required, and high containment research, diagnostic and vaccine manufacturing facilities and their output represent the backbone for any comprehensive disease control strategy.



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Conclusion

Countries that build and maintain bio-containment facilities:

- not only demonstrate vision and leadership,
- but also arm their nation and the world with precious know-how and much-needed resources to prevent the animal health disasters of the future.



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