Implementation of an HACCP model in foot and mouth disease control programmes

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Summary

The organisation and structure of the official Veterinary Services (OVS) are designed to meet a specific aim – the health certification of animal health, welfare and food safety in the production and processing stage. Disease prevention and control calls for programmes and projects that, depending on the characteristics of each disease, may involve any branch of the OVS, from the laboratory to field activities. For the purpose of this work, the model used is that of a country that is 'free from foot and mouth disease with vaccination' in accordance with the conditions stipulated in Chapter 8.8. of the World Organisation for Animal Health *Terrestrial Animal Health Code*. These conditions state that, to maintain this health status, a programme of monitoring and continuous control of the relevant variables must be implemented. This is achieved by applying good practice and identifying the critical control points in all processes, using a checklist that simplifies the task. The system that is developed can also serve as a guide for internal or external programme audits.

Keywords

Hazard analysis and critical control point – HACCP – Good practice – Disease control – FMD – Foot and mouth disease – Vaccination.

International trade in animals and animal products is facilitated by the adoption of international standards that are in line with the provisions of the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement) of 1995 (1). In this agreement, the World Trade Organization (WTO) delegated the World Organisation for Animal Health (OIE) to draw up the standards relating to trade in animals and animal products.

While the organisation and structure of official Veterinary Services (OVS) vary from country to country, they must all uphold the current international recommendations and standards established in Chapter 3.1. of the OIE *Terrestrial Animal Health Code* (*Terrestrial Code*) (2), which sets out the ethical, organisational, legislative, statutory and technical conditions and principles that must be applied.

Chapter 3.1. of the *Terrestrial Code* (2) stipulates that Veterinary Services should be able to demonstrate that they have appropriate legislation and an effective organisational structure; they must also be able to demonstrate that they have the human and financial resources that are needed to establish and apply the animal health, animal welfare and food safety measures that will enable them to issue international veterinary certificates of undisputed technical quality. To do this, it is essential that activities and processes, including the notification of diseases and/or health events, are regulated in a way that makes it possible to check that they are being carried out correctly.

The OVS channel their animal disease prevention and control activities through disease-specific programmes and/or projects. These activities cover the normative and regulatory aspects of laboratory and field work and include private sector participation through professional accreditation or activity-delegating systems. One of the main drawbacks of monitoring and controlling the various elements of these programmes is activity ‘sectorisation’, which is an issue that can be resolved by applying linear processes and identifying the critical control points (HACCP) of each stage and sector.

This article provides details of checklists that have been developed by the authors to make it easier to verify that the established procedures are properly applied and that supporting documentation is available to carry out self-assessment and improvement procedures so that assessments of certification procedures can be handled more effectively and so that auditors can systematise and simplify their task. The procedures include animal disease prevention and control programmes and good health practices applicable to the origin of the inputs, to the producer and processing establishments, and to the verification of the results obtained, primarily those regarding epidemiological surveillance.

For the purpose of this work, the model used is that of a country which is FMD-free with vaccination in accordance with the conditions stipulated in chapter 8.8 of the OIE *Terrestrial Code* (3) and which implements a monitoring and continuous control programme to maintain its health status by applying good practices and identifying the critical control points in all the processes from a purpose-designed checklist.

FMD prevention and control programmes with vaccination have three main elements: vaccination, including the inputs used and the manufacturing, control and shipping processes; vaccination of susceptible animals, including product transfer, application and registration; and, lastly, post-vaccination activities, including clinical and serological surveillance designed to demonstrate the effectiveness of vaccination, i.e. its ability to achieve or maintain official status (Fig. 1). All these activities are regulated and detailed in Chapter 8.8 of the *Terrestrial Code* (3), in this case for an 'FMD-free zone/country with vaccination'.

Thus, a full analysis of the system enables us to identify the main components, which are as follows:

– vaccine
– vaccination
– surveillance

As can be seen in Table I, the detailed analysis of the vaccine manufacturing process takes into consideration aspects such as the origin of the ingredients used to manufacture the vaccine, tests for the potency, purity and safety of the final product, and cold chain integrity throughout the process. To guarantee vaccine safety and quality, the analysis assesses to what extent these aspects comply with good manufacturing practices and with the international regulations laid down in Chapters 1.1.3., 1.1.6. and 2.1.5. of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (4). It should be noted that the official product and process controls are included.

In terms of issues related to vaccination, a number of critical points have been identified concerning the efficiency with which the immunogen is administered to animals and the responsibilities of the personnel in charge of each stage of the process. The points that have been identified are: maintaining the vaccine cold chain, the vaccination process and the registration and certification of the vaccine (Table II).

In terms of surveillance, it is necessary to monitor clinical and serological surveillance, animal movement control, and the resources allotted to simulation exercises and the contingency plan (Table III). The scheme also prioritises the most relevant aspects of the system in its various stages. Thus, for example, in a programme to control FMD with vaccination, priority must be given to determining vaccination coverage, which will depend on the capacity of the OVS to distribute and administer FMD vaccine in the susceptible population. But in a programme to prevent FMD through vaccination, which is an intrinsic feature of the 'FMD-free zone/country with vaccination' status, the protection level of the population, which is determined on the basis of the protective antibodies found in the susceptible population, indicates vaccination effectiveness. The absence of virus circulation is another indicator of choice for determining the population's health status.

This work scheme was tested during programme reviews in several countries. The results were highly satisfactory and gave rise to the production of standardised procedure manuals for various activities

that require review and control. This led to an improvement in the implementation, control and registration of specific activities. Likewise, it served as a preliminary step towards implementing good practices in health operations that are the subject of programmes or projects.

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References

1. World Trade Organization (WTO) (2013) – Agreement on the Application of Sanitary and Phytosanitary Measures. Available at: www.wto.org/english/docs_e/legal_e/15sps_01_e.htm (accessed on 10 March 2013).

2. World Organisation for Animal Health (OIE) (2015). – Chapter 3.1. Veterinary Services. *In* Terrestrial animal health code, 24th Ed. OIE, Paris. Available at: www.oie.int/index.php?id=169&L=0&htmfile=chapitre_vet_serv.htm (accessed on 15 October 2013).

3. World Organisation for Animal Health (OIE) (2015). – Chapter 8.8. Infection with foot and mouth disease virus. *In* Terrestrial animal health code, 24th Ed. OIE, Paris. Available in: www.oie.int/index.php?id=169&L=0&htmfile=chapitre_fmd.htm (accessed on 15 October 2013).

4. United States Pharmacopeia (USP) (2015). – Chapter 71: Sterility tests. Available at: www.pharmacopeia.cn/v29240/usp29nf24s0_c71.html (accessed on 4 August 2015).

5. Code of Federal Regulations (CFR) (2015). – Title 9: Animals and animal products. Part 113: Standard requirements. Available at: www.ecfr.gov/cgi-bin/text-

idx?SID=362ee89ea753e378ca357be9f6109b11&mc=true&node=pt9.1.113&rgn=div5 (accessed on 4 August 2015).

6. World Organisation for Animal Health (OIE) (2014). – Manual of diagnostic tests and vaccines for terrestrial animals, OIE, Paris. Available at: www.oie.int/en/international-standard-setting/terrestrial-manual/access-online/ (accessed on 4 August 2015).

7. Ahl A.S., Acree J.A., Gipson P.S., McDowell R.M., Miller L. & McElvaine M.D. (1993). – Standardization of nomenclature for animal health risk analysis. *In* Risk analysis, animal health and trade (R.S. Morley, ed.). *Rev. Sci. Tech. Off. Int. Epiz.*, **12** (4), 1045–1053.

Table I

Control of FMD vaccine production

Based on the vaccine production requirements of the World Organisation for Animal Health *Terrestrial Animal Health Code* (3)

For each control point, the checklist includes boxes for additional comments from the auditors (not shown here)

Controlled stage	Hazard	Detection	Expected result
Regulatory framework	Lack of national rules related to the production of vaccines and biosecurity and the requirement of GMP	Document check for monitoring both vaccines and biosecurity	Compliant with international standards (OIE)
Raw materials of animal origin	Introduction of exotic agents	Documentation and traceability to the source Certificates of supplier laboratory analysis	Verification that the countries of origin are free from exotic agents
Master cell banks	Cells of undetermined origin	Documentation with certification of origin	Verification of the source and certification of origin
	Contamination by bacterial and fungal agents	Test for sterility - microbiological tests for detecting viable bacteria and fungi (Ref. USP Ch. 71 [4] or other validated method)	No growth of bacteria or fungi detected
	Contamination by viral agents	Testing for adventitious viral agents (Ref. CFR 9. 113 [5], other national rules)	No adventitious agents detected: haemadsorbing, cytopathic or specific virus
	Mycoplasma contamination	Mycoplasma testing (Ref. CFR 9. 113 [5], other national rules)	No growth of mycoplasma detected PCR-negative
Primary viral inoculum bank	Virus origin not certified	Documents of origin. Certificates of approved establishments	Verification of the documents of the approved establishments
	Contamination by bacterial and fungal agents	Test for sterility (Ref. USP Ch. 71 [4] or other validated method)	No growth of bacteria or fungi detected

	Contamination by viral agents	Testing for adventitious viral agents (Ref. CFR 9. 113 [5], other national rules)	No adventitious agents detected: haemadsorbing, cytopathic or specific virus
	Mycoplasma contamination	Mycoplasma testing (Ref. CFR 9.113 [5], other national rules)	No growth of mycoplasma detected PCR-negative
	Cross-contamination due to heterologous FMDV	Identity and purity testing	Specific vaccine strain detected
Cell production	Bacterial and fungal contamination	Test for sterility (Ref. USP Ch. 71 [4] or other validated method)	No growth of bacteria or fungi detected
Virus production	Low performance virus	Control of infectivity titre – titre that infects 50% of exposed cell culture: TCID50%	Titre is ≥ the specifications and ≥ in the product documentation
	Contamination by bacterial and fungal agents	Test for sterility - microbiological tests for detecting viable bacteria and fungi (Ref. USP Ch. 71 [4] or other validated method)	No growth of bacteria or fungi detected
Inactivation	Deterioration of antigenic content	Determination of antigenic mass	Mass content is ≥ the specifications and ≥ that stated in the product documentation
	Incomplete inactivation	Validated inactivation kinetics control and inactivation control (negative passages on cells, FC and ELISA) (Ref. OIE *Terrestrial Manual*)	Kinetics must meet the specifications. Validated control of inactivation
Purification and concentration	Concentration failures	Determination of antigenic mass	Mass content is ≥ the specifications and ≥ that stated in the product documentation
	Bacterial and fungal contamination	Test for sterility (Ref. USP Ch. 71 [4] or other validated method)	No growth of bacteria or fungi detected
	Cross-contamination due to heterologous FMDV	Identity and purity testing	Specific vaccine strain detected

Aqueous phase formulation	Bacterial and fungal contamination	Test for sterility - microbiological tests for detecting viable bacteria and fungi (Ref. USP Ch. 71 [4] or other validated method)	No growth of bacteria or fungi detected
	Incomplete inactivation	Inactivation control (Ref. OIE *Terrestrial Manual*)	Validated control of inactivation
Emulsion	Inappropriate emulsification process	Emulsion stability testing (4°C and 37°C), physicochemical tests of the emulsion	Complies with product specifications, as well as with the documentation and regulation of the country of use
	Bacterial and fungal contamination	Test for sterility (Ref. USP Ch. 71 [4] or other validated method)	No growth of bacteria or fungi detected
Packaging	Bacterial and fungal contamination	Test for sterility (Ref. USP Ch. 71 [4] or other validated method)	No growth of bacteria or fungi detected
	Insufficient filling, and product loss	Check volume	Complies with product specifications and documentation
		Check that it is hermetically sealed (Ref. national or international pharmacopoeia)	Complies with pharmacopoeia
Finished vaccine (official control)	Sampling under official control and interdiction	Sampling, and taking (and sealing) counter samples. Prohibition certificate for the batch until results are received	Sample control, serial number and number of doses
	Potency failure	Direct testing (PD50, PGP) * 1 (biosecurity boxes) (Ref. Ch. 1.1.3. of the OIE *Terrestrial Manual)*. Indirect testing: serological tests, e.g. ELISA statistically correlated to protection	Complies with the country/OIE regulations
	Purity failure	NSP-Ab induction. ELISA test 30, 60 or 90 days post vaccination depending on the laws of each country	Complies with the country/OIE regulations
	Safety failure	Inactivation testing	Validated inactivation test

Security failure	Control in cattle (in vaccinated - revaccinated depending on the national legislation). Abscesses and adverse reactions	Complies with the country/OIE regulations
Other failures	Uniform process Poor emulsion stability Final product not sterile	Complies with GMP
Cross-contamination due to heterologous FMDV	Tests for identity and purity	Specific vaccine strains of the vaccine are detected
Bacterial and fungal contamination	Test for sterility (Ref. USP Ch. 71 [4] or other validated method)	No growth of bacteria or fungi detected
Lack of official approval Vaccine not approved during official control	Banned vaccine	Vaccine not approved and destroyed Certificate of destruction of vaccine not approved during official control

CF: complement fixation

CFR: Code of Federal Regulations

ELISA: enzyme-linked immunosorbent assay

FMDV: foot and mouth disease virus

GMP: good manufacturing practice

PCR: polymerase chain reaction

PGP: percentage of protection against generalised foot infection

PD: protective dose

NSP: non-structural protein

TCID: tissue culture infective dose

USP: United States Pharmacopeia

Table II

Vaccination control

For each control point, the checklist includes boxes for additional comments from the auditors (not shown here)

Vaccination control point	Hazard	Detection	Expected result
Vaccine control	Temperatures higher or lower than recommended (2°C to 8°C)	Maximum and minimum thermometer Number of doses matches both conservation device and ice Operational conservation device	
	Insufficient number of doses	Enough to cover animals to be vaccinated, considering the percentage of loss (usually 10%)	
	Expired vaccines	Expiry date checked	
	Lack of official approval	Checking stamping and approved batches	
Animal census	Census data error: incorrect data on susceptible herd Census data error: incorrect data on plant/owner	Determine the FMD-susceptible population Check records of plant/owner	The census data for determining vaccination coverage correspond to the herd to be vaccinated (data for vaccination coverage) The census data correspond to the owners/plants registered
Drawing up of certificates	Lack of documentation	Official sale certificate at the time of purchasing the vaccines	
	Completed incorrectly	Document inspection	Certificate of vaccination filled out correctly
	Incomplete certificate	Document check	Complete certificate of vaccination
Checking of vaccination elements	Insufficient equipment	On-site check	Automatic metal syringes Sufficient number of needles: 20 x 20 for adults (IM), and 15 x 18 for calves. For SC: 12 x 18 needles (1 needle every 50 administrations)
	Syringes in bad condition	On-site check	Functional syringes Supply of syringe components (plungers, washers, glass tubes, etc.)

Vaccination control point	Hazard	Detection	Expected result
	Contaminated equipment	On-site check	Clean disinfected equipment Be provided with hygiene items (bucket, brush, grid, virucidal disinfectant: citric or acetic acid (2%)
Vaccination	Improper administration	Operational control of vaccination	Proper syringe adjustment (dosage verification) Administration in the third upper part of the neck (IM or SC) Shaking of the flask Proper removal of air bubbles from the syringe Repeat administration if administered incorrectly due to movement Proper animal handling

IM: intramuscular

SC: subcutaneous

Table III

Control of surveillance

For each control point, the checklist includes boxes for additional comments from the auditors (not shown here)

Surveillance	Hazard	Detection	Expected result
Clinical surveillance			
Field	Presence of signs and lesions compatible with vesicular disease	Visual inspection	Animals without clinical signs
In markets and slaughterhouses	Presence of signs and lesions compatible with vesicular disease	Visual inspection	Animals without clinical signs
Notification/suspicion with laboratory tests	Notification/suspicion of vesicular disease	Samples submitted for diagnostic testing in accordance with Chapter 2.1.5. of the *Terrestrial Manual*	Negative suspicion
Determining of viral circulation and protective levels of the population by antibodies	Virus circulation and insufficient protective levels for the population	Application of surveillance in accordance with Chapter 8.8. of the OIE *Terrestrial Code* [3] and Chapter 2.1.5. of the OIE *Terrestrial Manual*	Absence of virus circulation and sufficient protective levels
Control of movements			
Fixed	Wrong documents, records, animal identification, origin and destination	Visual inspection and document check	Appropriate documentation
Moving	Wrong documents, records, animal identification, origin and destination	Visual inspection and document check	Appropriate documentation
Vaccination control (with records - vaccination coverage)	Insufficient vaccination coverage levels	Checking the vaccination records (vaccinated categories, number of establishments/vaccinated animals)	Sufficient vaccination coverage levels
Simulation exercises			

Table-top	Insufficient resources	Document verification	Resources allocated
	Exercises not done		Exercises done
Field	Insufficient resources	On-site verification	Resources allocated
	Exercises not done		Exercises done
Contingency plan	Error in contingency plan	Document verification	Existence of contingency plan

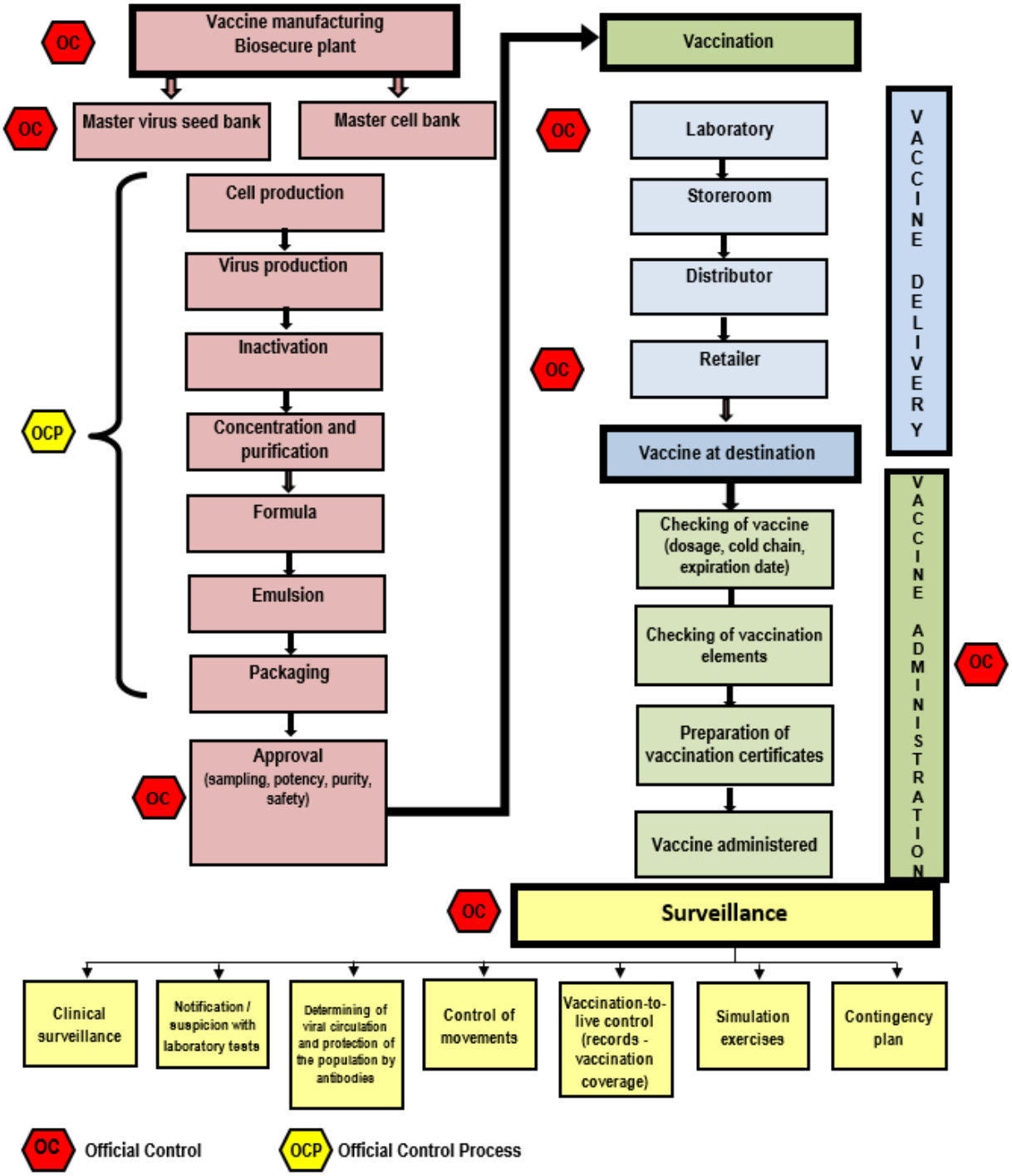

Fig. 1

Flow chart of the critical control points in vaccine production, vaccination and surveillance