Vaccine use – Vaccination strategies

FAO-OIE Global Conference on FMD Control

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Vaccine use & vaccination strategies

Vaccine use: basic considerations - 1

The choice of vaccination as a key tool to control FMD requires:
1. Vaccine storage and transport infrastructure,
2. Trained personnel in adequate numbers,
3. Necessary equipment (administrative & technical) and small technical materials for vaccine application.

VACCINE CONSERVATION:
- Permanent cold Chain: Cold rooms etc.
- Mobile Cold Chain: refrigerated lorries, ice boxes...

• Logistics for cold chain:
  • Vaccine shipment in insulated boxes with temperature indicators and coolant packs...
  • Evaluation of needs/ storage capacity/ delivery frequency...
• Good Management Practice for the Cold Chain – Quality Assurance.
  • Recording & Inspections, Operating Procedures ...
  • “First in, first out” – Respect of vaccine shelf-life, etc.
Confidence in vaccine potential shall not be eroded by misuse or unsuitable strategy.

At the best, vaccine shall be used:

a. In the framework of well-organized national campaigns with the consensus of all stakeholders

b. at least 90% of the targeted animals shall be vaccinated, branded and counted.

c. National individual identification of cattle is a must!
Vaccine use: basic considerations – 2 (continued).

- A vaccination campaign shall be short (1-3 months), massive without exceptions in view to synchronise immunity level.

- By precaution, campaigns are initiated when vaccine supply is secured as well as the entire logistical environment.

- Evaluation of the effects of a vaccination campaign shall be finished before starting revaccination.

- Agreement with vaccine manufacturers is recommended to make vaccine supply definitively not an issue in case of increasing demand.
COMMERCIAL PRESENTATIONS AND USES

1. Aqueous vaccines with saponine
2. Oil vaccines
3. Non purified versus purified vaccines
### COMMERCIAL PRESENTATIONS

**Different vaccine adjuvants for different uses:**

(vaccines with Marketing Authorisation)

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>Alhydrogel Saponine</th>
<th>Single Emulsion Oil in Water</th>
<th>Single Emulsion Water in Oil</th>
<th>Double Emulsion Water in Oil</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Route</strong></td>
<td>strictly <strong>S/cut.</strong></td>
<td>S/cut or I.M.</td>
<td>strictly <strong>I.M.</strong></td>
<td>S/cut or I.M. (I.D. in pigs)</td>
</tr>
<tr>
<td><strong>SPECIES</strong></td>
<td>Bovidae Sheep</td>
<td>Pigs</td>
<td>Cattle Sheep (pigs)</td>
<td>All Species</td>
</tr>
<tr>
<td></td>
<td>Goat</td>
<td>Goat</td>
<td></td>
<td>but mainly Pigs</td>
</tr>
<tr>
<td><strong>REGIONS</strong></td>
<td>Europe Africa</td>
<td>S.E. Asia</td>
<td><strong>South America</strong></td>
<td>S.E. Asia</td>
</tr>
<tr>
<td></td>
<td>Middle-East</td>
<td>Middle-East</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Antibody Kinetic 5 naïve cattle, 2 injections European Vaccine OAC (OIE Standard 3PD50) at T0 & T+6months. Adapted from JOUBERT - France - 1968.
Oil vaccine in cattle: oil vaccine, a slow release system.

Antibody kinetic from a group of ten cattle, after one injection of oil Vaccine (>6PD50) prepared starting from European Antigen Bank. Adapted from S.Cox - UK - 2008

Double Oil Emulsion-DOE

log10 VN titres type A homologous conditions

challenge

10 out of 10 protected without viraemia
Oil vaccine in pigs: oil vaccine, a slow release system.

**Vaccine use: Non purified vaccine versus purified vaccine.**

Colorimetric protein dosages before and after PEG purification of Antigens.

**Non Virion materials:**
- Ruptured BHK cells content
- Media components
- Markers of Infection-Non Structural Proteins of FMDV.

**Virion Materials**
- Capsid proteins
- 3D non structural protein

Equiv.1 dose O-A-C of S. America
3 treatments using PEG
**Vaccine use: Purified vaccine & NSP serology detecting antibodies specific of FMD infection**

Results by EITB method only.

Oil vaccine, 4 strains: O-A-C-Asia, max. Ag load (>OIE Standards)–24 cattle with 4 vaccinations within 42 days + challenge + serology after injections and 7 days post challenge including 2 challenge controls c & d.

Vaccine use: factors influencing results

1. Correspondence field virus / vaccine strain
2. Antigen payload drives efficacy
3. Influence of the time of revaccinations
4. Maternally derived Antibodies
Key factor N°1. : Vaccine /virus matching

Antibody Kinetic cattle n°1, in homo - heterologous conditions,
2 injections European Vaccine OAC Frenkel method OIE Standards at T0 & T+6months.

Adapted from JOUBERT - France - 1968
Key factor N°2: Antigen pay load drives efficacy

![Graph showing log10 VN titres type O over months with different Ag doses.]

Insecure zone

From Rweyemamu et al. 1984 - Alhydrogel –saponine vaccine
1. Low antigen payload or altered payload means LIMITED POTENCY and TRANSITORY IMMUNITY. High non altered antigen payload means HIGH POTENCY and LONG LASTING IMMUNITY.

2. OIE Terrestrial Manual recognizes methods either direct (PD50 & PGP) or indirect (EPP…) for measuring vaccine potency. All have 75% protection level as the lowest standards (3 PD50 or 12/16 cattle protected in PGP).

3. BELOW Standards, for a short time, vaccines prevent or mitigate disease in vaccinated animals, but not virus replication (with consequences as NSP antibodies induction or possible persistence of virus).

4. Federer in S. America (1967), then Hyslop experimentally have demonstrated, that development of so-called new “FMDV sub-types” was the consequence of continuous passages of virus in partially immunized animals (usage of inefficient vaccines).

5. “You’ll only be creating problems for yourself if you vaccinate with vaccines that do not comply with OIE Standards.”
Key factor N°3: influence of the time of revaccinations

Comparison of booster times in 2 groups of 5 naïve cattle
(European Vaccine -3 PD50) - Adapted from JOUBERT - France - 1968
MDA and Aqueous Vaccine

- By Augé de Mello et al. – 1989

- "Using oil vaccines calves can be vaccinated at about 2 month of age, when MDA level in many animals falls below protective values.

- Then, they can be revaccinated between 2 and 6 months in order to enter into the 6 month vaccination cycle which is recommended for cattle under 2 years of age.

- In this way the number of unprotected animals in cattle population can be reduced considerably."

Mean 59 Brazilian calves 1-4 month old
Nicholls et al. 1984

Type O
- No Vaccine
- Vaccine 1x
- Vaccine 2x

Days PV
Vaccination is one of the tools of the Global FAO/OIE Strategy for the Control of FMD.

A VACCINATION STRATEGY follows 2 successive phases:

1. **Primarily, a conceptual phase** involving stakeholders to create the larger possible consensus in the country to control FMD following the FAO-Progressive Control Pathway set of control stages.

2. **Secondarily, an executive phase** in the field with actors following instructions and procedures.
In the lower stages of the Progressive Control Pathway for FMD, in particular **Stage 2**, a good start in vaccination strategy is a targeted and well organized **national vaccination program** to limit the effects of FMD in a certain area or animal sector(s) or sub-sector(s).

- A targeted vaccination could for instance be aimed at protecting the **dairy sector especially in peri-urban areas**…

- or in the **high producing herds** (cattle feed lots – intensive pig production premises…).

- Development of **Public Private Partnership (PPP)** for vaccine delivery and use.
Vaccination strategies at the PCP Stage 2

Case of endemic countries where vaccination is not controlled:

1. **Private vaccination programs** in high producing herds with veterinarians,
   - responsible for defending premises against FMD external contamination
   - Ordering / handling directly international vaccines on premises
   - Managing vaccinations according to their *own private programs*
   - Inviting international consultants in case of problems.
   - > High consumption of vaccine doses = **Over vaccinated herd**

2. **Public vaccination programmes** (uncertain) in small farm sector,
   - Vaccination operations absent or uncertain, depending on government money.
   - No FMD control measures,
   - Small farm sector being the virus reservoir of the country.

*To unify theses two very different sectors in the same programme should be the aim of Stage 3*
Vaccination strategies at the PCP Stage 3

- **In the stage 3 of the Progressive Control Pathway for FMD**, vaccination strategy should be more aggressive and under the exclusive responsibility of the government,
  
- A well organized vaccination program shall eliminate FMDV in a certain zone of the country.
  
- In this zone, vaccination tactics extend the vaccinated area from key herds to all susceptible livestock.
  
- Vaccination programs are refined according to vaccino-surveillance results.
  
- FMD control program may be endorsed by OIE.
  
- Development of Public Private Partnership (PPP) for vaccine delivery and use shall reach an optimal level.
Starting with PCP Stage 3 up to the highest levels, mass vaccination shall be regularly implemented for several years.

Consequently,

- Mandatory vaccination shall be in the national law
- Injection of vaccine should be performed preferably by vaccinators/veterinarians paid by government.
- Injection should not be delegated to farmers without guaranties about reality of injections and appropriate storage of vaccine vials.
Targeted vaccination to stop epizootics progression
Several examples in Asia Minor threatening Europe
Targeted vaccination stage 3: Buffer zone.
A successful example: Turkish Thrace 1963-1998
Turkish Thrace Buffer Zone stopped the following exotic viruses:

- SAT 1 Arabia 1962 virus
- A22 Iraq 1964 virus
- Asia-1 Iran 1973 virus
- Asia-1 Turkey 1983 virus
- Asia-1 Turkey 2000 virus
Targeted vaccination stage 3: Ring vaccination

An example of successful coordinated strategy for FMD control in the Balkans – 1996 (3 countries) by EU & FAO.

Albania – May 1996
*Infected zone: stamping out
* Vaccinated zone: 2 rounds mono-valent vaccination in 50km radius.
* Surveillance zone

FYRO Macedonia – June 1996
*Infected zone: stamping out
* Larger Vaccinated zone: 2 rounds vaccination extended to zone 1 & Kosovo.
*Surveillance zone: large with strips along borders.

No infection detected in vaccinated zones.

from Leforban et al. - 2003
Vaccine use & vaccination strategies

- Ring vaccination is almost always performed:
  • around an infected zone where stamping out is carried out.
  • with a surveillance zone designed around the vaccinated zone.

- Ring vaccinations **without** stamping out of infected animals are rarely published.

- **Success of ring vaccination** associated with stamping out was observed in Europe (Leforban):
  • in Bulgaria in 1991
  • In the Balkans in 1996
  • In Turkish Thrace, Bulgaria and Greece in 1996.

**In every cases the vaccine was made from the European antigen bank**
Targeted vaccination stage 3: Uruguay
Curbing and extinguishing an epizootic episode in 2001.

from V. Saraiva - PANAFTOSA

23 April
FMD
1st. Case
East area

Ring Vaccination
East region

Mass Vaccination 1
East > Central > West

Mass Vaccination 2nd
East > Central > West

Foci number

16 Aug.
FMD
last cases
European*, Asian*, African* & S. American* countries have succeeded to control or to eradicate FMD thanks to strategies using regular campaigns of mass vaccination.

**Major key factors for such successes are:**

- **Mandatory vaccination** once (Europe) twice (S. America) a year in cattle only (with identification).
- **Vaccination coverage above 90%** including calves (>4m.).
- **Vaccines controlled by government** and refused batches destroyed,
- **Vaccines injected by vaccinators** or veterinarians (Europe)
- **Purified vaccines used for DIVA Strategy** (S. America).
- **In case of FMD, stamping out** and fair compensation.
- **Convincing information to farmers for active participation.**
- ...

*refer to other speaker presentations*
Failures in vaccination strategies

MOST FREquent CAUSES of FAILURES:

Vaccine quality: too much vaccine used remains of inadequate quality to maintain a durable immunity (6-12 months).

Delivery systems also often fail to vaccinate animals before they are first traded (as calves), exposing these animals to infection in transit or the market place, and spreading infection through the marketing chain to new regions.

Combination of poor quality, poor timing and poor coverage results in gaps that allows infection to circulate. Confidence is therefore eroded, among veterinarians as well as stakeholders.

Vaccine supply is definitely an issue because:

- inactivated vaccine production cannot easily be scaled up,
- whereas S. America with a huge over-capacity for vaccine production cannot supply other continents in the world.
3 key factors to control successfully FMD in your country:

1. “Selecting vaccine batches of certified potency (OIE standards) with approved strains used in appropriate conditions is the first step to solve your problems”.

2. Stage by stage compliance with the FAO Progressive Control Pathway for FMD control is the second step towards success.

3. Endorsement of FMD control programs by OIE is the third step for final success.
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Thank you!

Michel Lombard