Why is the OIE waiting period to return to trade doubled for vaccination to live?

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At an April 2011 meeting of QUAD CVOs in New Zealand a working group was tasked to conduct a review of the scientific literature on the use of FMD vaccines for emergency purposes.
In a nutshell

Recovery of free status

1. When an FMD outbreak or FMDV infection occurs in an FMD free country or zone where vaccination is not practised, one of the following waiting periods is required to regain the status of FMD free country or zone where vaccination is not practised:

   a) three months after the last case where a stamping-out policy and serological surveillance are applied in accordance with Articles 8.5.42. to 8.5.49.; or

   b) **three months after the slaughter** of all vaccinated animals where a stamping-out policy, emergency vaccination and serological surveillance are applied in accordance with Articles 8.5.42. to 8.5.47. and Article 8.5.49.; or

   c) **six months after the last case or the last vaccination** (according to the event that occurs the latest), where a stamping-out policy, emergency vaccination not followed by the slaughtering of all vaccinated animals, and serological surveillance are applied in accordance with Articles 8.5.42. to 8.5.47. and Article 8.5.49., provided that a serological survey based on the detection of antibodies to nonstructural proteins of FMDV demonstrates the absence of infection in the remaining vaccinated population.

Vaccinate-to-die

Vaccinate-to-live
Core Project Team

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Collaboration with International FMD Strategic Reserves NETWORK; EU FMD; IAH, Pirbright

Desirable Outcomes

- Removal of economic impediment for vaccinate-to-live strategies
- Timely decision making regarding FMD vaccination
- Global reduction of mass culling of livestock through vaccination in a FMD outbreak
Project components

History of trade restrictions or waiting period

Vaccinology

The carrier state

DIVA tests – Characteristics and limitations

Post vaccination surveillance

Live animal versus animal product trade
The current OIE recovery waiting periods in Article 8.5.9 of 3, 6, 12, and 24 months reflect considered scientific opinion, precedence and historical practicalities (6 months dates back to 1971) rather than having a specific scientific basis.

From 1968 to 1992 (24 years) of the Code’s existence, animals & animal products from countries free with vaccination moved equivalently to those free without vaccination (6 months after last outbreak)
Since 1992 there has been a separation of the waiting periods by SCAD into 3 month blocks for countries free without vaccination and 6 month blocks for those free with vaccination.

Concepts of FMDV *infection* and FMDV *circulation* replaced the previous notion of *disease* in 2002/3 to distinguish surveillance objectives and intensity for *FMD country not practising vaccination* and *FMD country practising vaccination* respectively.
Recovery waiting periods for FMD free without vs FMD free with vaccination

Article 8.5.9.

Recovery of free status

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   a) three months after the last case where a stamping-out policy and serological surveillance are applied in accordance with Articles 8.5.42. to 8.5.49.; or
   b) three months after the slaughter of all vaccinated animals where a stamping-out policy, emergency vaccination and serological surveillance are applied in accordance with Articles 8.5.42. to 8.5.47. and Article 8.5.49.; or
   c) six months after the last case or the last vaccination (according to the event that occurs the latest), where a stamping-out policy, emergency vaccination not followed by the slaughtering of all vaccinated animals, and serological surveillance are applied in accordance with Articles 8.5.42. to 8.5.47. and Article 8.5.49., provided that a serological survey based on the detection of antibodies to nonstructural proteins of FMDV demonstrates the absence of infection in the remaining vaccinated population.

   Where a stamping-out policy is not practised, the above waiting periods do not apply, and Article 8.5.2. or 8.5.4. applies.

2. When an FMD outbreak or FMDV infection occurs in an FMD free country or zone where vaccination is practised, one of the following waiting periods is required to regain the status of FMD free country or zone where vaccination is practised:
   a) 6 months after the last case where a stamping-out policy, emergency vaccination and serological surveillance in accordance with Articles 8.5.42. to 8.5.47. and Article 8.5.49. are applied, provided that the serological surveillance based on the detection of antibodies to nonstructural proteins of FMDV demonstrates the absence of virus circulation; or
   b) 18 months after the last case where a stamping-out policy is not applied, but emergency vaccination and serological surveillance in accordance with Articles 8.5.42. to 8.5.47. and Article 8.5.49. are applied, provided that the serological surveillance based on the detection of antibodies to nonstructural proteins of FMDV demonstrates the absence of virus circulation.

3. When a FMD outbreak or FMDV infection occurs in a FMD free compartment, Article 8.5.6. applies.
Currently, for vaccinate-to-live in a *FMD free country not practising vaccination* surveillance must substantiate absence of FMDV *infection* [Article 8.5.9 1 c) ] which is more stringent than vaccinate-to-live in a *FMD free country practising vaccination* surveillance which must substantiate absence of FMDV *circulation* [Article 8.5.9 2 a)] yet both have the same waiting period of 6 mos.
Higher potency emergency vaccines (6pd50) confer benefit in terms of rate of protection, duration of immunity and effect against local virus replication and transmission compared with conventional vaccines.

A series of statistically designed experiments provided unambiguous proof that higher potency FMD vaccine could reduce and even inhibit subclinical infection and reduce the likelihood of persistence (Barnett et al 2004).
Conventional vaccines have no such proof in the scientific literature.

No unequivocal experimental evidence that conventional vaccine reduces susceptibility to infection, virus excretion or duration of persistent

Early effective reduction in virus excretion with higher potency emergency vaccines administered at the earliest possible time prior to challenge breaks the infection chain in less than half the time as that of conventional vaccines and thus exponentially reduces the amount of FMDV in the environment.
Must assure that basic aspects of emergency vaccination affecting population immunity such as:

- maternal antibody have been conducted.
- incorrect storage,
- application,
- inadequate coverage,
- insufficient match,
Persistent Carriers:

The risk of transmission from carriers to susceptible animals is anecdotal (9 times in 150 years) and has never been substantiated experimentally yet cannot be totally excluded.

This risk led to the recommendation, added in 2006, that live vaccinated animals not be imported into an FMD free country not practising vaccination (i.e. vaccinates can NOT be traded with another FMD free country not practising vaccination in Article 8.5.12. (3)).
Article 8.5.2 already states that, every year a country claiming to be an FMD free country where vaccination is not practiced, no vaccinated *animal* has been introduced since the cessation of *vaccination*.

If transmission by convalescent non-vaccinated carriers is an infrequent phenomenon then the risk of a vaccinated carrier is considerably lower, probably close to zero and thus the risk of a carrier vaccinated with higher potency vaccine even closer to zero.
Persistent Carriers:

It is the African buffalo carrier with SAT2 serotype that has maintained the carrier concern.

It is postulated that certain FMDV isolates establish persistence efficiently, while others may even lack the ability to establish persistence.

Transmission was observed in only 4 of 36 experiments between 1950 and 2005: 2 with carrier African buffalo to cattle; 1 African buffalo to African buffalo; and 1 carrier cattle to susceptible pigs.

No cattle to cattle transmission has ever occurred experimentally.
Of commercial NSP assays, the Cedi test (now PrioCheck), PANAFTOSA and IZS Brescia perform best for vaccinated carriers with Se approaching 90% and Sp exceeding 99% in cattle with improved performance when used in series.

NSP Assays are considered reliable on a herd level (Clavijo, 2004) and have been used successfully in South America for over a decade.

Lack of NSP assay validation in species other than cattle is a concern.
Se for vaccinated pigs ranges from 44 to 69%.

Results for sheep have too few animals (less than 10) for generalizations.

Performance in deer/wildlife is unknown.

High potency vaccines are more purified so should have better performance but no experimental proof.

DIVA validated at the herd level (appropriate for products) but lacks Se for individual animal level (OIE already restrict trade in live vaccinates).
SURVEILLANCE:

Each country must justify their post outbreak surveillance including sero-surveillance statistical parameters to the ad hoc Group for Evaluation of Country Status for FMD when reapplying for OIE FMD status in addition to the Code 3 or 6 mos. waiting periods.

In March 2006, that ad hoc Group noted that there should be a substantiation of the statistical certainty of the absence of infection or circulation (OIE, 2006).

Such statistical certainty is the foundation for a threshold of surveillance evidence paradigm replacing the current waiting periods of 3 and 6 mos. blocks of time (proposal under development for EU by Angus Cameron & associates, 2012)
The risk of FMDV in products derived from higher potency vaccinated animal is virtually zero, certainly significantly less than for routinely vaccinated products from a FMD country practising vaccination where the OIE has Articles with conditions for safe trade [Article 8.5.17 (semen), 8.5.21 (embryos); 8.5.23 (beef); 8.5.24 (pigs and other ruminants); Article 8.5.27 (milk/milk products)].

The OIE does not now specify any additional risk mitigation measures for a FMD free country not practising vaccination once status is regained after 6 months.

There is no evidence that the risk is any difference in the risk at 3 months than it is at 6 months.
Additional risk mitigation measures can be negotiated bilaterally to meet individual country’s ALOP in an analogous manner to those currently in place that allows the importation of deboned meat from a FMD free country practising vaccination to a FMD free country not practising vaccination in Europe and North America.
Animal Products: [Commodity based trade]

Additional trade measures could include:

- restriction of vaccination to a protection zone to enhance credibility of a FMD control programme;
- animal identification and traceability;
- permanent vaccinate movement restrictions;
- restricted to bovine products as DIVA validation is lacking in other species;
- restricted only for protective vaccination (not suppressive);
- +/- serology before and after vaccination document the absence of FMDV challenge; and the development of carriers;
- absence of potential wildlife reservoirs etc.
Conclusions

Current science supports eligibility to return to OIE status of *FMD free country where vaccination is not practised* in 3 months (mos.) following an outbreak where stamping-out and higher potency emergency vaccination is applied irrespective of whether vaccinate-to-live or vaccinate-to-die policies are used [i.e. align waiting periods in Code Articles 8.5.9.1 b) & c)].

The alignment of the 3 mos. waiting periods applies only to all animal products and live *unvaccinated* animals.

The 2006 Code restricted export of live vaccinated animals to a *FMD free country not practising vaccination*. 
Conclusions

It is surveillance intensity rather than time that establishes the risk of the presence of residual FMDV.

The OIE rather than stipulating a 3, 6, 12 or 18 mos. waiting period in Article 8.5.9, should set an acceptable level of statistical certainty for surveillance to (i) substantiate the absence of FMDV infection for a *FMD free country where vaccination is not practised* OR (ii) substantiate the absence of FMDV circulation for *FMD free country where vaccination is practised*. 
Next Steps

• Determined at QUAD Animal Health Group, April 2012
  • Invitation to present the concept to the Ad Hoc FMD working group revising the OIE Code chapter committee in Paris, July 3-5/ 2012
  • Formal submission of the documentation to support the Code change to OIE by a member country, Dr John Clifford on behalf of the QUAD countries on August 17, 2012
    • Resulting in referral of documents to ad hoc FMD Working group for incorporation into FMD Code chapter revisions with review by the joint SCAD & Code Commissions in February 2013 (potential distribution to members prior to next general session in May 2013)
  • Publication of the OIE submission on the IAH, Pirbright website for the International FMD Vaccine Strategic Reserves Network
  • Invitation to present at Open EUFMD as first plenary speaker in Spain, October 29, 2012
Article 8.5.9

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   c. 3 months after the last case or the last vaccination (according to the event that occurs the latest), where a stamping-out policy, emergency vaccination using higher potency FMD vaccine not followed by the slaughtering of all vaccinated animals and serological surveillance are applied in accordance with articles 8.5.42. to 8.5.48., provided that a serological survey based on the detection of antibodies to nonstructural proteins of FMDV demonstrates the absence of infection in the remaining vaccinated population.

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Questions