GFRA Gap Analysis Workshop Report

Hanoi, Vietnam, 20-22 October 2015

Global Foot-and-Mouth Disease Research Alliance

FMD Policy Meets Science

Scenario development and session moderator: David Paton

Interactive discussions on topical policy issues to discuss whether there are gaps in knowledge that could be filled by research to the benefit of policy development.

Participants were invited to join one of three break-out groups discussing the disease control scenarios below. A facilitator introduced each topic, collated the outcome of group discussions and fed this back to the full meeting in plenary.

Scenario	Background	Facilitator
1) Following use of emergency vaccination without slaughter in a FMD affected area of a PCP stage 3 country, what other control measures are most important and for how long should they be maintained?	It is a truism that FMD vaccination alone is rarely sufficient without other measures to reduce transmission, but in many countries with communal herds, conventional movement controls are very difficult to implement	Nick Lyons Aldo Dekker
2) What is the optimal regime for emergency vaccination of pigs in response to an outbreak of FMD?	In Korea, there has been discussion over whether incomplete protection of vaccinated pigs stems from poor vaccine match or sub-optimal vaccination regime. Many FMD experts outside Asia are unfamiliar with vaccination of pigs in the field.	Young Lyoo, Don King
3a) As a country that buys vaccine via a tender process, how do you establish what is an acceptable post-vaccination serology titre for post vaccination monitoring? 3b) What post vaccination monitoring (PVM) is appropriate for use in a FMD free zone without vaccination after use of emergency vaccination?	Vaccines are invariably used to protect against heterologous virus challenge. But in most cases the correlation between heterologous antibody titre and protection is not known. PVM can improve confidence in the effectiveness of emergency vaccination and provide additional confidence to trade partners complementing or replacing the need for NSP serosurveys.	David Paton Wilna Vosloo

Recommendations arising from discussion of scenario 1

Key considerations: (i) What are the risk factors for ongoing transmission in an area using emergency vaccination? (ii) What other measures are needed for control? (iii) How do we understand how to target these control measures?

Considering:

- Current potency tests in cattle and efficacy tests in sheep and pigs provide good evidence of vaccine efficacy
- The relation between antibody response and protection has been shown in various species, with most data available in cattle
- Most countries applying prophylactic vaccination do not use serological tests to evaluate vaccine potency, nor vaccination efficacy in the field
- The level of outbreak reporting is low in most FMD endemic countries
- Emergency vaccination around outbreaks is often not practiced in countries using prophylactic vaccination
- Strategic revaccination of animals that are moved from areas that are facing outbreaks in a country that is using prophylactic vaccination is often not practiced.

The group recommends:

1. Countries using prophylactic vaccination should test every batch of vaccine in a small group of animals before it is applied in the field.
2. Countries should apply currently available tools are needed to help with the identification of outbreak strains, such as serotype specific penside tests to identify if the outbreak is caused by a serotype not present in the vaccine. But also collaborate with reference laboratories that can do genetic and antigenic characterisation.
3. Serological surveys are needed in vaccinated areas to determine if the vaccine response in the field is similar to the response at batch testing. When an outbreak occurs, serological studies in risk areas (neighbouring villages) are necessary to determine the vaccination status and the need for revaccination.
4. Research on risk assessment is needed in the context of movements of animals, networks, hubs, modelling, where are the hot spots and to review value chain analysis, taking into account the implemented control measures, vaccine induced antibody titres in the field, number of outbreaks and spread due to various transmission routes (see points 1 - 3). Based on these data an indication of the antibody titre needed in the field can be determined in relation with the antibody titre determined in potency tests.
5. Socioeconomic studies are needed to develop suitable incentives for implementing movement controls, taking into account the possibility of early movement after revaccination.
6. Studies in risk communication will help to maximise awareness of stakeholders

Recommendations arising from discussion of scenario 2

Key considerations: Observed low efficacy of vaccines in swine could reflect (i) Regime used (timing and frequency of vaccination); (ii) Formulation of oil vaccines; (iii) Inadequate match of antigen used in the vaccine. A literature review of pig vaccination could be helpful.

Considering:

- There are almost no published studies comparing adjuvants for pigs with respect to protection.
- Although the best antibody response is seen when vaccinating in absence of maternally derived antibodies, there are studies that indicate that active immunisation is possible in the presence of maternally derived antibodies.
- All vaccine matching tests are performed in cattle, matching of vaccines could be different in pigs
- Due to limited availability of data on vaccine efficacy in pigs, limited data are available on the relation between antibody response and protection. The limited studies available show however that similar to cattle there is a significant relation between antibody response and protection.
- Limited studies on use of alternative routes of vaccination in pigs are available.
- No standard test for vaccine efficacy in pigs is available
- Limited studies into passive immunisation in pigs show limited effect of passive immunisation.
- Disinfection works only at temperatures above 0 °C, no data are available on combinations of antifreeze and disinfectant at low temperature.

The group recommends:

1. Research on evaluation and screening of alternative adjuvants for vaccination in pigs
2. Research on effective (improved) vaccination regimes to generate optimum protection in pigs to accommodate maternal antibody responses (to reduce the immunity gap)
3. Research on optimized (or calibrated) vaccine matching tests for infection in pigs
4. Research on reliable lab tests (ELISA) to measure protective immune responses in pigs (particularly heterologous responses to field viruses - see scenario 3)
5. Research on validation of alternative routes (IM, SC, ID) and sites of vaccination (to minimize local tissue granulomas in valuable meat cuts) and even multiple sites (with divided dose)
6. Research on impact of interference between components in multivalent vaccines?
7. Research on develop specific parameters for vaccine batch release for use in pigs
8. Research on explore passive immunisation in pigs to generate transient immunity?

An additional gap not related to vaccination that became apparent during recent Korean outbreaks:

9. Research on effective disinfection protocols for low temperatures?

Recommendations arising from discussion of scenario 3

Key considerations: Protection is influenced by many variables relating to the properties of the vaccine used, the vaccination regime and the nature of virus challenge that occurs in the field.

Measuring protection requires use of serological tests for which the correlation to protection is also affected by multiple factors. Scenario 3b was not discussed due to lack of time. The soon-to-be-released post vaccination monitoring guideline from OIE/FAO will provide advice and options to help address some of these uncertainties

Considering

- Serology provides very useful correlates of protection as determined in potency tests. But the relation between antibody response and protection is different for different vaccines, different vaccine formulations, different routes of vaccination and different times after vaccination
- The relation between antibody response and protection in potency tests is different from the relation between antibody response and protection in the field.
- There is limited data on the effect of concurrent infections on protection induced by FMD vaccines.
- The relation between antibody response and protection is often not validated in newly developed serological tests.
- Countries that use prophylactic vaccination do not sufficiently evaluate the antibody response in the field.
- Countries that use prophylactic vaccination do not sufficiently evaluate the duration of the immunity after vaccination.

The group recommends:

1. Research on the actual determinants of immunological protection for better prediction of protection under different circumstances without the need to establish correlations in advance using specific potency tests that match these circumstances.
2. Comprehensive field studies on antibody response and vaccine efficacy, e.g. a detailed longitudinal follow-up of vaccination campaigns in endemic settings.
3. Research on the impact of other diseases and vaccinations on the development of FMD immunity.
4. Vaccine users should work closely with vaccine producers and would benefit if as well as advice, they received appropriately calibrated reference sera or test kits to help determine the expected threshold of vaccine-induced immunity.
5. Research on relation between protection and antibody response in newly available, commercial serology kits that detect structural protein antibodies.
6. Countries that use prophylactic vaccination should determine what proportion of the population has responded in the expected way to a vaccine. This type of straightforward survey should always be performed on a large scale to identify problems in vaccine delivery, whilst complementary studies to look at aspects of protection such as its duration and the impact of antigenicity should be performed on a small scale to augment understanding of the main survey.