**Serological monitoring of FMD vaccination: Principles and Practise**

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Population immunity serosurveys can address two related but different objectives. Firstly, they can help to determine how well vaccination has been carried out and secondly, how well the target animals are likely to be protected from disease. Ideally, the first objective requires knowledge of how animals respond to correctly administered vaccine under the conditions of a particular target species, background immunity, vaccine batch, vaccination regime, post-vaccination sampling interval and test methodology. The second objective requires knowledge of how the antibodies that are measured corelate with protection against the threat posed by the specific viruses circulating in the field. In practise, precise knowledge of different outcome determinants and their influences is often missing, and so assumptions and simplifications must be made. For example, there is often information about antibody responses and sometimes about protection against vaccine homologous viruses, 3-4 weeks after a single dose of vaccine has been given to a naïve steer. However, the expected level of antibody or protection is less clear at other time periods, against other field viruses, and in animals with different vaccination and infection histories. This talk will discuss the pros and cons of different compromises with a view to making the best use of the options that are available.

**A new model for independent FMDV vaccine QA/QC as an aid to vaccine selection**

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Relationship coefficients ($r_1$-values) are often used to understand the antigenic relationship between a foot-and-mouth disease (FMDV) field strain and a vaccine. Values greater than 0.3 are suggestive of a close antigenic relationship between the field isolate and the vaccine strain; potent vaccine containing the vaccine strain is likely to confer protection. While $r_1$-values are often useful and highlight antigenic trends (such as the antigenic mismatch of the A/ASIA/G-VII field isolates with current vaccines) they have their limitations. To carry out $r_1$-value work one needs the vaccine virus from the vaccine company. In addition, the test is based on monovalent bovine serum collected 21 days after a single vaccination. However, in FMDV endemic countries, vaccines often contain multiple strains, and a booster vaccine is required to achieve appropriate antibody levels against circulating field strains. To overcome some of these limitations we are proposing a new model for FMDV vaccine QA/QC with the aim to roll this out at AU-PANVAC in Africa. This model does not require the vaccine virus or monovalent bovine serum. Instead, a reference panel of viruses is identified and tested against sera that have been obtained from animals vaccinated with commercial, often multi-strain, vaccine used in the field. Multiple vaccines are tested against the reference panel and by assessing the neutralisation titres the most suitable vaccine and testing regime can be determined. This talk will consider the benefits and limitations of these different serological approaches to vaccine selection and consider how this new model could be implemented in other regions.

## *In vivo* testing of vaccines in South East Asia – how well does antigen matching correlate with protection?

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Antigenic matching data are generated *in vitro,* for a quick analysis of the emerging viruses against available epidemiologically relevant FMD vaccine strains. This method has advantages such as speed of analysis, cost, and most importantly, circumventing animal ethics considerations. It provides a relatively easy and rapid way to test the suitability of available vaccine strains against a large number of field isolates and a statistical estimate to predict protection ($r_1$-value). However, interpretation of data can be challenging, especially in heterologous systems, where the $r_1$-value is not always a good indicator of vaccine efficacy. In such cases, testing of vaccines *in vivo* in target hosts and challenge with a representative heterologous field virus ($r_1$-value <0.3 by VNT) can provide valuable information on vaccine efficacy. Such studies also provide insights into the pathogenicity and infectiousness of novel variants of FMDV. Due to the costs incurred and ethical implications, many of these live virus challenge studies were/are performed as collaborations between laboratories and data shared to inform on decisions on vaccine strains to be included in vaccine banks or for routine use in the field.

Over the last 10 years a number of laboratories have investigated vaccine efficacy using the major commercially available vaccines in cattle, pigs and sheep against endemic and variant viruses from the A/Asia/SEA-97 and O/ME-SA/Mya98 lineages that have been circulating in South East Asia (Pool 1). In addition, *in vivo* testing was also performed against the newly introduced O/ME-SA/Ind-2001 lineage. Although the A/ASIA/G-VII lineage has not been found in SEA so far, the eastward spread of the O/ME-SA/Ind-2001 lineage has given concern that such novel lineages may also be introduced from neighbouring geographical pools.

In most cases, emergency vaccines that contain high levels of antigen (>6$PD_{50}$/dose) provide protection against clinical disease, decrease the clinical signs, and lower the amount of virus excreted as well as duration of excretion into the environment. This is despite low $r_1$-values in some cases. Therefore, even if animals are not fully protected, vaccination can be a useful additional control measure to minimise spread and economic damage. This presentation will give an overview of some of the *in vivo* vaccine efficacy trials and discuss the results.

**Novel FMD Vaccines and Their Future Use in Developing Countries**

Elizabeth Rieder

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Foot-and-mouth disease (FMD) is endemic in many developing countries mainly in Africa and Asia, significantly affecting livestock productivity. This can lead to weight loss and decrease in milk production as well as restrictions imposed on trading which severely impacts commerce and development in affected areas. Chemically inactivated, oil adjuvanted FMD vaccines are critical to FMD control in endemic countries. Although these vaccines are effective in inducing protective immunity in livestock species, the response is short-lived with limited cross-protection and are unable to eliminate virus from persistently infected animals. The use of live virus requires expensive high containment biosecurity level 3 facilities for production. To address the shortcomings of inactivated vaccines, current efforts are devoted to develop novel recombinant vaccines including marker inactivated vaccines, empty capsids, recombinant protein vaccines, and synthetic peptide vaccines. Here I will review the progress on experimental and advanced development stages of these vaccine platforms and how they could support global FMD control and eradication.

**Official control of Foot-and-Mouth disease vaccines**

David Mackay

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Official control authority batch release ("official control") is the process by which regulatory authorities confirm that vaccines released onto their national markets comply with the specifications that are set during the process of approval for licensing (also termed registration or marketing authorisation). Official control generally relies on a combination of review of the batch records provided by the manufacturer and re-testing. The emphasis placed on these two aspects varies between regions and between regulatory authorities. As it is not usually possible to replicate the full range of in-process and final products tests that are performed by the manufacturer, where re-testing is carried out, the aim is to independently verify the key parameters of the vaccine that determine its quality, safety and efficacy. In the case of FMD vaccines the tests to be performed are described in Section 4 of Chapter 3.1.8 of the OIE Manual of Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (the OIE Manual). For FMD vaccines the primary concerns relate to confirmation of innocuity to demonstrate freedom from live FMD virus and potency. Independent confirmation of potency represents a particular challenge in the case of FMD vaccines. The definitive test is the *in vivo* challenge test in cattle as described in the OIE Manual. *In vitro* alternatives involving testing of sera from vaccinated animals may be used, provided that the cut-off in the test has been validated with respect to the minimum acceptable potency defined in the authorisation. The ability of regulatory authorities to independently evaluate potency is greatly facilitated by cooperation with manufacturers to gain access to the protocols, vaccines strains and reference sera used to validate and perform the manufacturer's batch potency test.