Vaccination in support of official FMD-freedom

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www.pirbright.ac.uk

Country/zone free from infection with FMDV where vaccination is practiced. Articles 1.11.2., 1.4.6., 4.18., 8.8.4.

- Compulsory systematic vaccination in target population
- Vaccine complies with standards in Terrestrial Manual
- Evidence for >24mths of implementation and supervision of surveillance measures as described in Terrestrial Code (1.4.6., 8.8.43.)
- Vaccination in accordance with Terrestrial Code 4.18. (vaccination chapter)

- Description of
  - Relevant legislation
  - Vaccine characteristics and suitability
  - Target species
  - ID of vaccinated animals
  - Recording/certification system
  - Coverage and population immunity monitoring
  - Date of last vaccination

What, why, how, when, findings, follow-up….

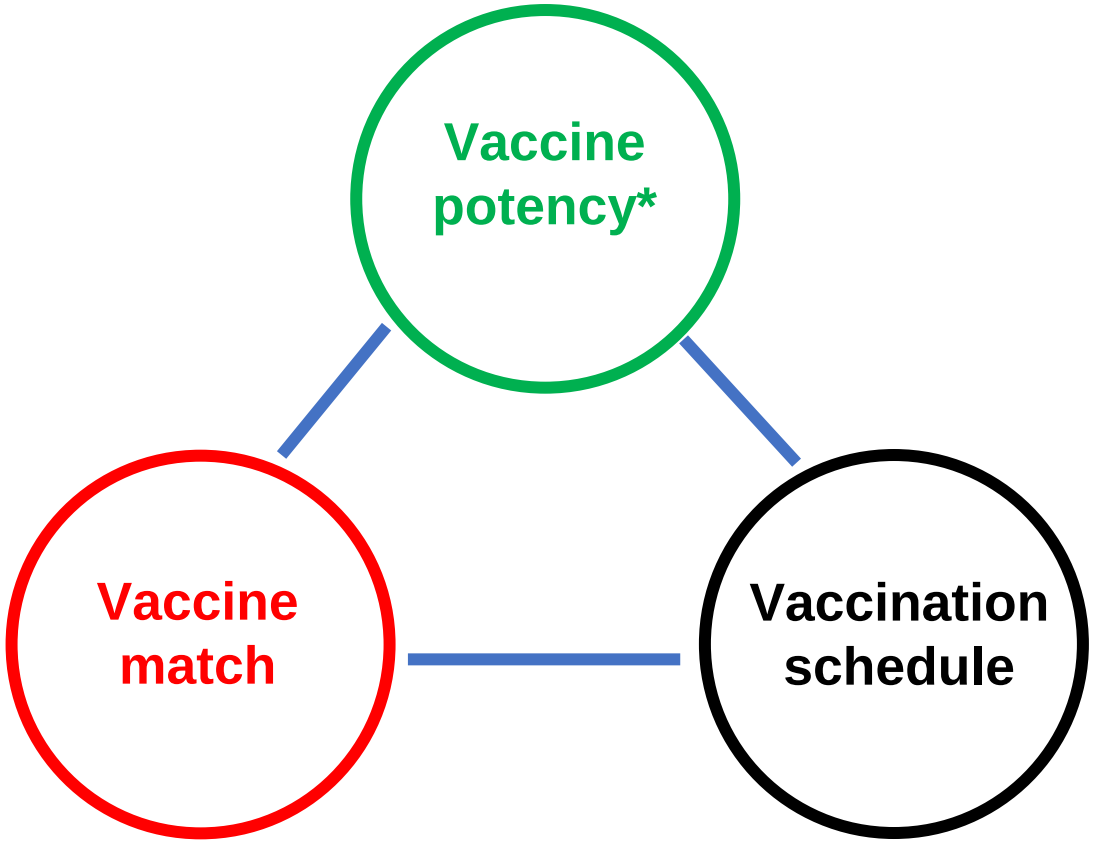
FMD vaccine problems

FMD vaccines have a number of limitations including:

- short duration of immunity;
- antigenic diversity - different vaccine strains needed for different field virus strains;
- low thermal stability.

Whether or not an FMD vaccine induces protective immunity depends on three main factors:

- the potency of the vaccine at the point of use;
- the degree of antigenic match between the vaccine strain and the field strain;
- the vaccination schedule;
- overall protection reflects their combined effects **as well as synergy with other measures (biosecurity, movement controls, etc).**

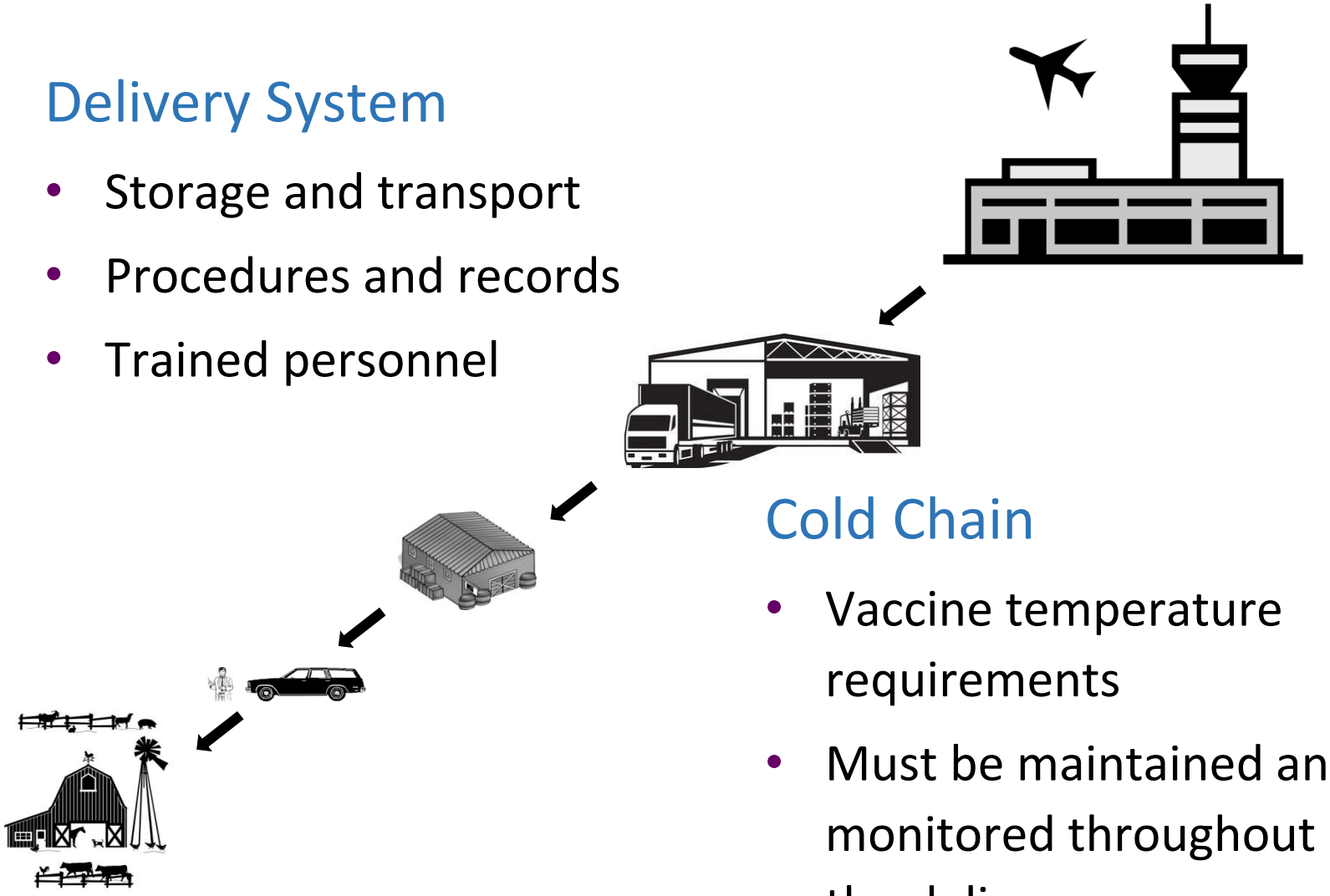


*potency = strength of elicited protective immunity, principally determined by amount of intact antigen and adjuvant

Operational challenges of a vaccination campaign

Delivery System

- Storage and transport
- Procedures and records
- Trained personnel

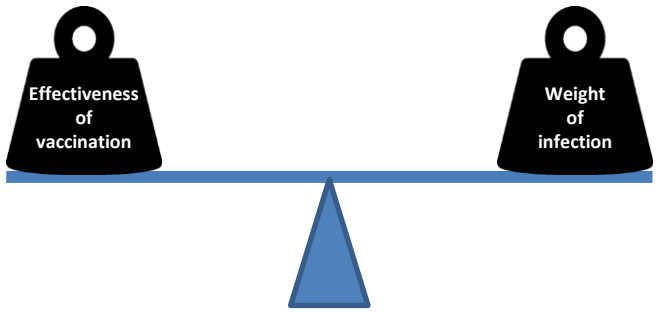


Cold Chain

- Vaccine temperature requirements
- Must be maintained and monitored throughout the delivery process

Continued FMDV Transmission despite vaccination

With possible masking of disease reducing the value of clinical surveillance

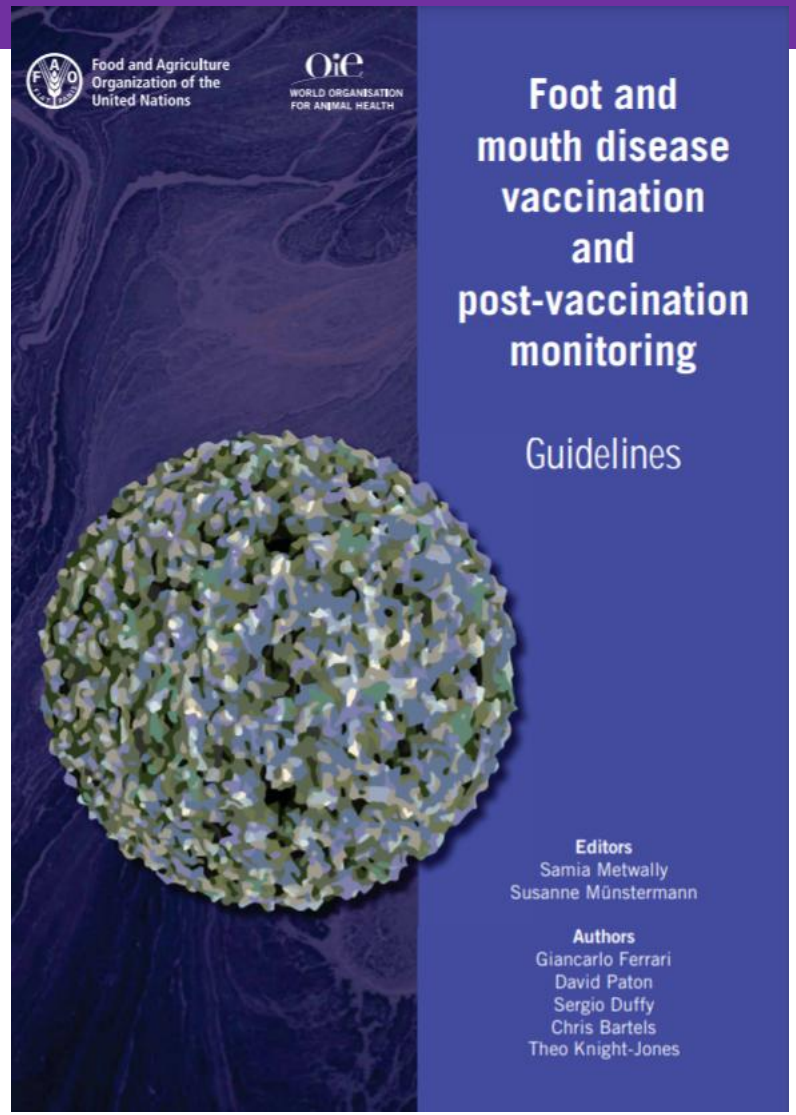


Inadequate immunity
Poor vaccine quality or match
Vaccination too late
Insufficient animals correctly vaccinated

Complementary controls inadequate
Delayed detection and/or response
Poor surveillance
Zoosanitary failings

Monitoring vaccination

- Why is it necessary
- Implementation
  - Strategy and regimen
  - Procurement
  - Cold chain audits
  - Coverage estimates from records or surveys
  - Population immunity serosurveys
- Outcomes
  - Reductions in clinical cases
  - NSP serosurveys of undisclosed infection
  - Investigating vaccine failure



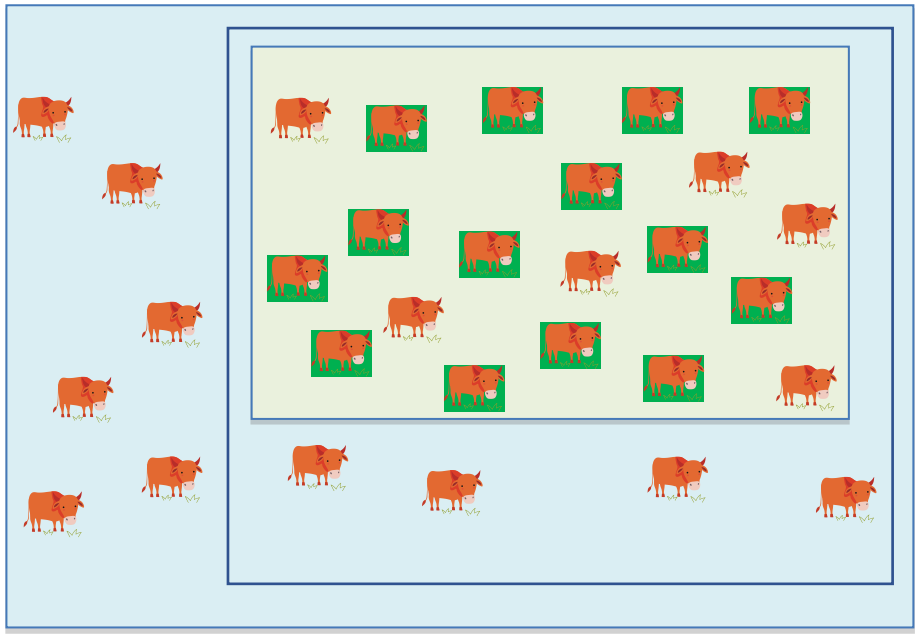
https://www.fao.org/3/i5975e/i5975e.pdf

Vaccination coverage

Transparency

- Need clarity on methodology used to calculate denominator and numerator data
- Results should be stratified to account for differences between campaigns, species, ages of animals and regions

Synergy with population immunity results



Vaccine coverage can be expressed as:

20/24 = 83%

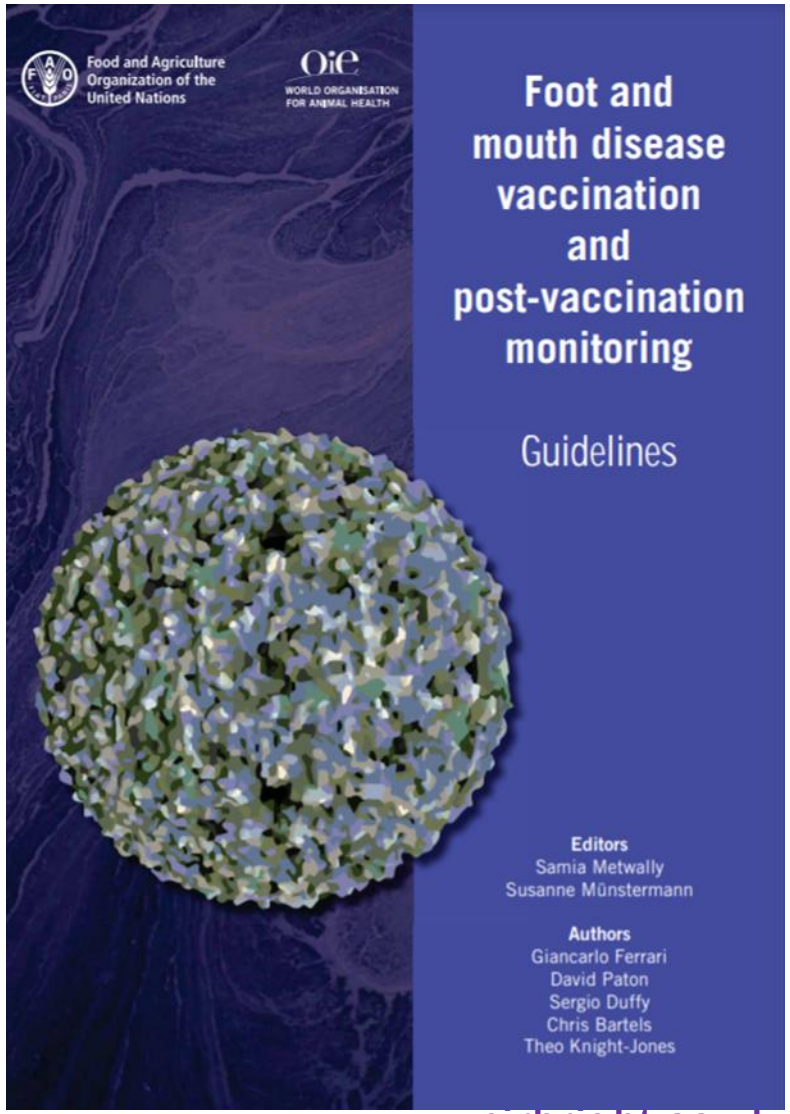
or

20/30 = 67%

Population immunity surveys

Survey design should be explained and justified if different from WOAH standards

- Two stage sampling design recommended
- Timing in relation to vaccination
- Stratification by species, age and region
- Immunity target threshold at herd or animal level
- Justification for test cut-off



The correlation between serology and homologous protection from potency tests

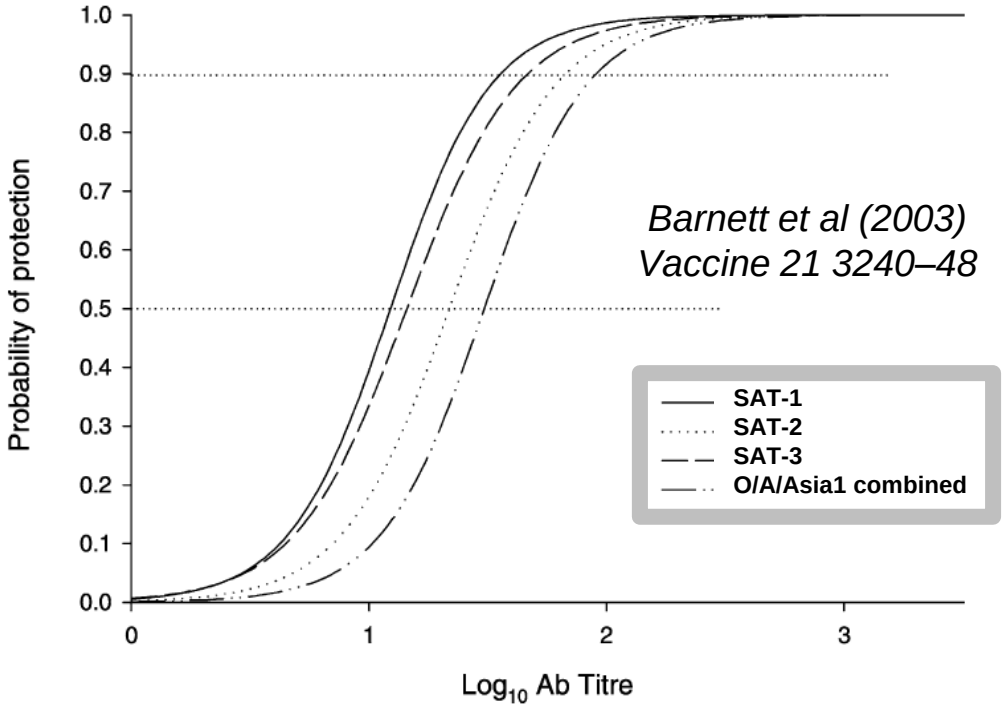


Fig. 2. The best fitting models to four different subsets of the data.

Establish serological correlates of protection from live challenge tests in support of registration.

Subsequent vaccine batch release can be based on immunogenicity studies to see if vaccines elicit the Ab threshold indicative of the desired level of protection

Same thresholds can be used in population immunity studies with certain caveats

Titre for 75% probability of protection (T_{75}) for O/A/Asia1 combined ≈ $\log_{10}1.7$ (1 in 56) in VNT
(But the VNT is not very reproducible!)

Population immunity studies

Two post-vaccination intervals:

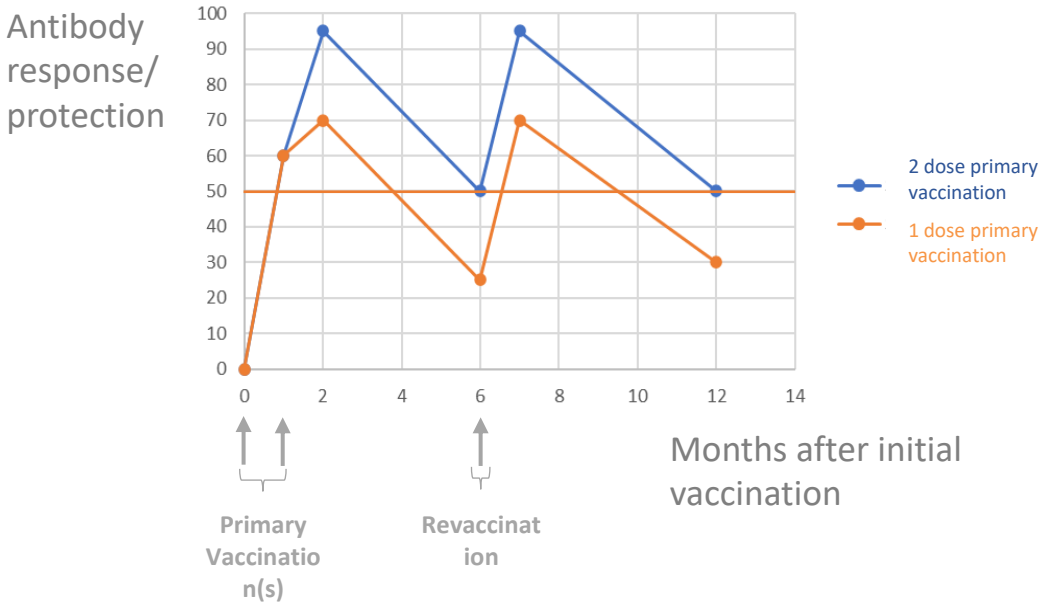
Estimating the immune status at point of vaccination

(measures residual immunity);

Estimating the immune status shortly after vaccination

(measures peak immunity).

Schematic Representation



Combine with a longitudinal study of a smaller cohort to understand dynamic rise and fall of antibodies with time after vaccination

Choice of serological threshold

- Consistent with expected response for the vaccine in question
  - Use batch release sera from manufacturer as a standard
  - Create own standards from a small trial
- Consistent with likelihood of protection against a homologous or heterologous challenge
  - Use test and threshold established by challenge tests supplied by manufacturer
  - Use cross-neutralization against field virus threats (ref lab)

Immunity survey to support disease freedom (1)

- PVM guideline assumes Se/Sp = 100%
- Can compensate by reducing the acceptable error and the expected prevalence of protected animals in each category, which increases the sample size
- For example:

  Confidence = 95%

  Acceptable error = 7.5%. (calculated prevalence plus, minus 7.5%)

  6-12 months: Expected prevalence of protected = 55%

  12-24 months: Expected prevalence of protected = 70%.

  > 24 months: Expected prevalence of protected = 80%

Immunity survey to support disease freedom (2)

The number of epidemiological units (EU) and animals to be sampled per stratum would be as follows:

6-12 months: 60 EU and 5 animals per EU (total samples 60x5 = 300)
12-24 months: 58 EU and 4 animals per EU (total samples 60x4= 240)
> 24 months: 45 EU and 3 animals per EU (total samples 60x3= 180)

May omit 0-6 month category if not interested in maternal immunity estimates and because some may not be vaccinated.

For practicality and to ensure that the number of EU and animals sampled will be approximately correct, 65EU and 5, 4 and 3 animals per category could be requested (12 animals per EU, 780 total samples per stratum). Should allow a good estimate of the level of protection of the animals per category but also an idea (not precise, but approximate) of the level of protection of the EU.

Presenting the information for a dossier or questionnaire

Extract from report of *AHG Evaluation of FMD status of Members/October 2018*

Guidance document on presentations of applied survey design and results for applicant OIE Members for official recognition of FMD free status

https://www.woah.org/app/uploads/2021/09/a-ahg-fmd-oct2018-web.pdf

1) Objectives of the survey (e.g. detecting infection, prevalence estimation, population immunity, etc.)
2) Survey design:
   a. Reference population (by species and area)
      - Total number of animals
      - Definition of an epidemiological unit
      - Types and description of different epidemiological units
      - Number of epidemiological units, and where possible location of epidemiological units
      - Indicate how the reference population relates to the target population
   b. Strategy for survey
      i. Indicate if one stage or two stages
      ii. Stratification and criteria for eligibility (according to age, size of epidemiological unit, etc.)
      iii. Method for sample size calculation
      iv. Parameters that influence sample size calculation:
         - Design prevalence: between and within epidemiological units (for sample size calculations of epidemiological units and animals)
         - Level of confidence
         - Level of precision (where relevant)
         - Laboratory test sensitivity and specificity
         - Herd sensitivity and specificity (where relevant)
      v. Details on the method of selection of epidemiological units and animals (random, convenience, targeted, etc.)
      vi. Description of laboratory tests performed; cut-off values used to determine positive results and their sensitivity and specificity (and whether validated or assumed)
      vii. Timing of sampling indicating time period/dates and other relevant information (e.g. in relation to vaccination or disease risk)
      viii. Description of follow-up of serological findings

Presenting the information for a dossier or questionnaire

1) Results

   i. Deviation from original plan
   ii. When, where and how many samples were actually taken
   iii. Particularly for NSP surveys provide:
      - Tabulated results, broken down to epidemiological units showing animals present, animals sampled and results (indicating preliminary and confirmatory testing) including the dates of the farm visits and overall results (see an example in the Annex)
      - A break-down of the results by age group including those that tested positive and those that tested negative.
      - Maps showing locations of epidemiological units in the reference population, those sampled and those with positive results
      - Details of control measures and epidemiological enquiries as part of the survey.
   iv. For population immunity studies
      - Tabulated results by administrative division (or other suitable geographical division), serotype, age group, post vaccination interval and herd size if available.

2) Conclusion in relation to the objective and compliance with provisions of the *Terrestrial Code*

Follow-up in case of uncertain or problematic findings