Regional Vaccine Matching Results and Recommendations Regarding to Sample Submission

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INTRODUCTION

Vaccine matching

- Characterization the antigenic relationship between field strains of a specific serotype to a vaccine strain (known to convey protection against a broad spectrum of subtypes of that serotype)
  - Means that: to determine how antigenic “SIMILAR” the field virus is to the vaccine virus.

Vaccine matching has to purpose;

- Firstly to chose the most effective vaccine for use in a particular circumstance and

  - Secondly to monitor, on regular basis, the suitability of vaccines maintained in vaccine antigen reserves
Importance of Vaccine Strain Selection

The two most important vaccine related determinants that the vaccine can afford an adequate protection:

1. how well it can induce a strong immunity = Potency;
   to ensure the vaccine can be effective in the event of an outbreak of FMD

2. How closely related it is to the field virus against which protection is desired = Antigenic / vaccine matching;
   to identify the antigenic deviation and to select a new vaccine strain from suitable candidate one
Antigenic Diversity

- Antigenic change due to mutation and recombination
  - During the replication of viruses, mistakes occur in the coping process of viral nucleic acids. These are known as mutation.
  - RNA viruses, like FMDV, generate a higher rate of mutation than DNA viruses, since there is no effective proof-reading mechanism for RNA viruses.
- Genetic drift: the progressive accumulation of random genetic mutation; may or may not resulted changing amino acid.
- If this genetic code of amino acid changing is resulted in altered antigenic characteristic; ANTIGENIC DRIFT
  THIS VIRAL EVOLUTION CYCLY IS RESULTED NEW ANTIGENIC VIRUS STRAINS
- It is also considered the reason of antigenic changing: Major disease outbreaks in properly vaccinated animals and reduced efficacy of vaccination.

Importance of Vaccine Matching/ Why it needs?
Stage of Vaccine strain selection

- **Field work**: investigation outbreaks and collection samples
- **Lab work**: determination the serotype, strain and vaccine matching
- **Vaccine producer**: produce and supply the vaccine
- **Livestock industry / competent authority**: determining the vaccination policy and purchasing vaccine for use / banks
- **Overall decision making process and international dimension**
Methods Used for Vaccine Matching

**In-vivo evaluation for cross protection-Challenge Study**
- Requires 30+ days for single immunisation and longer time for revaccination
- Expensive
- Impractical when large volume of samples to be analysed

**Lab-based Vaccine Matching**
- **Sequence based alternatives to serology:** Primary genetic profiling by sequencing
- **Serology:** Selecting representative field isolates for antigenic matching; current the most available lab test used in routine
- **Antigenic Cartography:** New approach, serological antibody from vaccination measured and then generating two dimensional map using a process called “antigenic cartography” so that antigenic evolution can be determined

**Field measurements of vaccine effect**
- Post-vaccination serology
- Vaccine effectiveness study
Vaccine Matching by Serology-R1 value testing

- Two serological tests are currently used for VM:
  - Virus neutralisation test (VNT):
  - Liquid phase blocking ELISA (LPBE):
- Measuring the antigenic similarity between the field isolates and vaccine strains by comparing the cross reactivity of a vaccinal serum against these two virus
  - The results expressed as:

\[
\frac{\text{Ab titre of ref. serum against field isolates}}{\text{Ab titre of ref. serum against vaccine strain}} = r1
\]

- Interpretation: VNT: cut-off: \(r1 \geq 0.3\); LPBE: two steps cut-off: \(r1 \geq 0.2 \rightarrow <0.4\); \(r1=0.4\)
  - 0.4 to 1.0 protection expected
  - 0.2 to 0.39 some protection expected
  - <0.19: not protected
- Vaccine matching is not obtain a precise results e.g. lack of field samples, vaccine strains and reagents, lack of information about vaccine strains, tests are not harmonised… etc
- A disadvantage of the ELISA method is that it is harder to standardise the virus antigen concentration used in the test. Currently, because of unavailability of LPBE reagents suited for non all vaccine strains, LPBE has been not used routinely
## TYPE-O/Vaccine Matching Results for 2012 by WRL

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# TYPE-A/Vaccine Matching Results for 2012 by WRL

## Type A:

Vaccine matching studies for type A FMDV by VNT-WRL FMD

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<th>A Sau95</th>
<th>A Tur06</th>
<th>A Ind 17/8 2</th>
<th>A May9 7</th>
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### TYPE-Asia-1 / Vaccine Matching Results for 2012 by WRL

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<th>WRL Sample Ref</th>
<th>Asia1 IND 8/79</th>
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**Number Of vaccine matching achieved in 2012**

(20 out of 35 were collected in 2011)

- **TYPE O**: 16
- **TYPE A**: 11
- **TYPE ASIA-1**: 8
- **TOTAL**: 35

**Distribution Vaccine matching Achieved 2012 by Country**

(6 isolates from ME countries)
## Vaccine Matching Results for 2012 by Şap Institute

<table>
<thead>
<tr>
<th>Sublineage that belong to the field isolates</th>
<th>Vaccine Strain and Reference Sera</th>
<th>O TUR 07</th>
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Assessment $R$ value Results

• It is not enough making a decision for changing vaccine strain with single or a few low $r$ value results.
• In this cases, this should be consider as a important caution and carefully follow it up
• It needs more sample from different region and taking account also outbreak investigation results for vaccine failure
• Protective $r$ value results should be also analysis to evaluate vaccine suitability
• If $r$ value results are always fluctuated in range of weakly positive, this is also critical for vaccine suitability
Protection 'Windows' Conferred by Homologous and Heterologous FMD Vaccines

Adapted from Pay, 1994

by Tim Doel, Merial Animal Health
Sampling Strategy for effective vaccine matching

✓ Specific recommendations are difficult to make about the numbers of samples that should be collected and analysed from regions with endemic infection.

✓ The optimal number will depend heavily on the prevailing circumstances and resource constraints.

✓ Guidelines on the intensity of sampling should be set regionally, within a defined FMD control program that takes account of local conditions.

✓ However, principally samples represent:
  • enough number
  • outbreak situation
  • all region
  • regular base
  • along with field information for vaccine efficacy and outbreak investigation.

• Therefore, within ecosystems, it is important to ensure that there are no unexplored gaps where unknown variants may hide undetected.
Gaps on Sampling and Transportation

Sample submission has some constrains currently:

- Due to the regulation by IATA, international transport of specimens for FMD diagnosis has been constrained.
- Compliance with the rules for carriage by air was therefore difficult and costly, and restrictions often created unpredictable delays in transit, during which the virus present in samples could become inactivated.
- Preservative solutions can be added to samples to maintain the integrity of the nucleic acids for genome sequencing, even after prolonged storage without cooling.
- However, current methods, other than the addition of glycerol, make recovery of the infectious virus difficult for testing vaccine matching.
- For some consideration like a lack of openness about disease reporting or willing to test them their own lab, not all countries are willing to send samples to international reference laboratories.
CONTROL MEASURES IN WEST EURASIA CAUSING DIVERSITY!

How much can we implement control measures for FMD in WE?

Diagnosis FMDV- reaching every single outbreak then sampling and serotyping? = Not really!

Outbreak Investigation (understanding disease spread dynamics; source, severity, impact…)? = ?maybe as a pilot study

Quarantine (Restriction, biosecurity, desinfection…)? = Partially, not effective!

Registration and recording then monitoring? = Not all country!

Control of animal movement and trade (Market, biosecure movement)? = Not effective!

Stamping out/Culling? = Not practised yet!

Preventive vaccination = The most relevant used control tool in WE, but not enough coverage and effective!

SO WE SHOULD THINK ABOUT IT!

POOR CONTROL MEASURES AND POOR VACCINATION MIGHT BE FORMULATED MORE GENETIC AND ANTIGENIC DIVERSITY

APPLIED VACCINE IN THE REGION SHOULD BE POTENT, EFFECTIVE AND BE ENSURED WELL MATCH WITH CIRCULATED FIELD VIRUS
CONCLUSION and RECOMMENDATION

- Poor control measures has been resulted antigenic diversity in the region
  - Needs developing control strategy fully operated
- Vaccine match is one component of vaccine efficacy:
  - If vaccine match is imperfect, vaccine quality may compensate
- Predicting vaccine match is a key surveillance task
  - For a perfect vaccine matching mecanism, it must be carried out a perfect outbreak surveillance program
  - Improve monitoring in the field and target surveillance
- It needs standardization of existing methodologies and FMD vaccine matching training
  - It needs developing on laboratory methods so that they can speed up vaccine matching tests and make them more reliable
- It needs regional co-operation mechanism
  - identify regional vaccine strains
  - Creating a reference sera panels suits with regional vaccine strains for vaccine matching
  - More sharing of matching reagents, viruses and vaccines
CONCLUSION and RECOMMANDATION

- It needs prospective field studies to look at vaccine effectiveness directly including influence of vaccine match; at the moment Turkey has initiated a vaccine effectiveness study program aimed conducted each year for per vaccine serotype
- Needs a further investigation on the relationship between r1 values and protection efficiency- different potent vaccines and revaccination?
- It needs a consensus for decision on changing vaccine strain when detecting poor matching versus continuing vaccination by high potency vaccine
  - OIE Standard: For routine prophylactic purposes FMD vaccine should contain at least 3 PD50 per protective cattle dose
  - Research fact: A coverage of 100% should be the objective (3PD50 vaccines will only protect 75-85% of cattle; Dekker, 2008).
  - Challenge Study results for Asia-1: Asia-1 Shamir vaccine can protect to current circulated virus matched poorly with Asia-1 Shamir vaccine when the vaccine is high potency
  - Current situation for vaccine insufficiency: Available vaccine in market is less than half needing for susceptible population in the region
- Therefore we need a consensus on how to achieve target of protective level of the population in the region!
CONCLUSION and RECOMMANDATION

 IT IS CLEAR THAT THERE IS CRITICAL GAPS FOR CURRENT VACCINE MATCHING MECHANISM IN THE REGION:
   Delay vaccine matching testing; 20 out of 35 isolates were collected in 2011, but r value results were available in 2012; some of them after one year later
   Number of available vaccine matching results is not enough; only 35; 6 of them from ME
   There is no follow up action for poor matching results; for example. Poor type A vaccine matching results in 2007 samples from Afg, revealed decision for vaccine strain changing in 2008- and latest type Asia-1
   There is no vaccine matching laboratory serviced in local base
   Constraints on transportation samples is one of the critical obstacle for speed up getting results earlier
SPECIFIC RECOMMENDATION FOR FUNCTIONAL VACCINE MATCHING MECHANISM

• Creating local laboratory/laboratories to carry out testing routinely and in time
  – To launch test system, it needs a local training program
  – Developing a reference sera panels for testing r value
• Campanied with early detection program proposed in the region;
  – Collected at least ten sample from each country
  – First serotyping and genetic analysis these sample
  – After according to serotyping and genetic analysis results, testing enough number of sample by r value VNT
  – Each sublineage circulated in the region should detected by genetic analysis and then antigenic characterization should be done by at least several samples for each sub lineage
  – Along with samples outbreak investigation information should be collected
  – New approach field base vaccine effectiveness study should be introduced to per country- it is also useful in favour of understanding the disease spread dynamics and assessment of vaccine implementation process in the field