GF-TADs
GLOBAL FRAMEWORK FOR THE PROGRESSIVE CONTROL OF TRANSBOUNDARY ANIMAL DISEASES



VACCINE POTENCY REQUIREMENTS IN WEST EURASIA REGION

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Discription of PD50:

- FMD vaccines are routinely evaluated using the protective dose of 50% **(PD_{50})** test;
  - Certain number of animals, dividing three groups, are given different doses of vaccine .
  - Animals are given a standard dose of FMD virus injected into the tongue.
  - Animals are observed for foot lesions.
  - From these data, the fraction of the standard dose of vaccine that would protect 50% of exposed cattle is then estimated.
  - The reciprocal of this is the **PD_{50} value**.
  - This is a measure of ***vaccine potency***, reflecting protective efficacy.

International Standart for Vaccine potency

There are three major standard describing potency:

1.World Organization for Animal Health **(OIE);** Manual of diagnostic tests and vaccines.

2.European Pharmacopoeia**(Ph.Eur.);** Monograph 04/2005:0063 (Ph.Eur., 2006).

3. European Commission (**EC);** (Council directive 2003/85/EC).



International Standart for Vaccine potency (2)

Based on these standards:

- The quality and suitability must comply with the requirements laid down by Monograph 04/2005:0063 of the European Pharmacopoeia
- Standard potency vaccine are formulated to contain sufficient antigen to ensure that they **meet at least the minimum potency requirement of the Ph.Eur.** (3 PD50)**(Ph.Eur.)**.
- For routine vaccination programmes in countries and zones recognised as free from FMD with vaccination or in FMD endemic areas a **3 PD50** (minimum) potency level is **required (OIE2006).**
- The latest revisions of OIE Manual of diagnostic tests and vaccines states that **6 PD50** per cattle dose is **preferred**.
- However, for an FMD vaccine batch to be eligible for use in emergency situations within the European Member States, the PD50 content must be greater or equal to 6 **(Council directive 2003/85/EC).**

Review on Vaccine potency

- ✓ FMD vaccines traditionally represent the largest share of the veterinary vaccine market worldwide in terms of sales, with 26.4% of the entire livestock biological business (Gay SG et.al)
- ✓ ***Potency is a major concern with FMD vaccines.***
- There are primarily three formulations in all commercial inactivated FMD vaccines worldwide:
  - High-potency vaccines (emergency use)
  - Oil-emulsion conventional vaccines (routine control)
  - Aluminum hydroxide vaccines (for cattle)

Review on Vaccine potency (2)

Higher potency vaccine;

✓can be expected to induce a rapid onset of immunity within 2-3 days of vaccination,

✓induce higher and more durable level of antibody

✓a wider spectrum of relevant strains following a vaccination

✓The case for using higher potency vaccines is clear, including greater protection against heterogeneous strains, a quicker onset of immunity, and increased protection from viral shedding and transmission.

✓The latest revisions of OIE Manual of diagnostic tests and vaccines states that six protective dose 50 (PD_{50}) per cattle dose is preferred.

✓However, this is not an absolute requirement owing to the acceptance that this would significantly reduce the number of vaccine doses which they are used and production capacity in worldwide .



Review on Vaccine potency (3)

- >3 PD50 potency vaccine are recognized as **fit-for-purpose** when consistently used in **endemic settings** in view of controlling **clinical disease**
- Oil-adjuvanted vaccines with 3 PD_{50} potency provides protective immunity within 7 days in cattle, swine and sheep.
- Vaccines decrease clinical disease, and virus amplification , but do not prevent the persistent infections (Alexandersen S et.al).
- a higher antibody response reported for double oil-emulsion(Smitsaart E et.al).
- Oil-adjuvanted vaccines are the most used worldwide but, in order to maintain sufficient levels of immunity to suppress occurrence of clinical disease, re-vaccination must be carried out every 6 months.
- After multiple doses of vaccines in older animals, vaccination frequency could be decreased to once a year, provided that no new strains not covered by the vaccine formulation emerge or are introduced (Mattion N. et.al).



Evaluation of potency test influence on potency value

One of the main characteristics of the Ph.Eur. vaccine potency test:

- is its intrinsic statistical variability due to the small groups of animals used test.
- This variation means: a 10 PD50 vaccine range from approximately 4.5 to 22 with 90% confidence limits
- without taking account of the biological variation of animals to FMD vaccination and live virus challenge (Doel, 2003).

> '(i) how reliable is a PD50 value based on one potency test when the test system itself suffers from low precision and
>
> (ii) how effective will a vaccination scheme be in the field, where biological variation will have an influence as well?'.

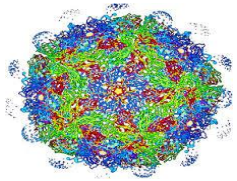
- ***In other words, is a PD50 value of 6, based on the outcome of a single potency test, significantly different from 3 or even 10 PD50?***



Potency test requirements_European Pharmacopoeia

FMD Virus Challenge 21days post.vacc.

PROTECTED (absence of clinical signs on feet)



50% protective dose

3 PD50 minimum requirement

6 PD50 or more for

3 groups of 5 cattle

each group vaccinated with a specific dose volume e.g. 1/1,1/4,1/16

Alternative approaches, such as challenge-free serological potency test can be used; if it is correlated with challenge test.

Role of Disease Manager and Manafucturer

- Disease managers should establish board for vaccine marketing authorization and develop regulation
- It should be create a mechanism for control of vaccine through a national vaccine reference laboratory
- Batch potency test important for new antigens or new combinations of antigens.
- Then this should be continued before delivery for each batch
- Manufacturer conduct definitive potency test is by challenge in cattle or acceptable serological test
- A separate authorization should be required for each FMD vaccine produced by manufacturer.



Results of survey on vaccine potency requirement conducted in WE

- Responses from 6 countries were received.
- Weighted of the data from 6 responses is not enough to justify on requirements for vaccine potency.

Country	Pop.size;LR/SR	Vacc.available; prod. or purchased	Vaccine used/doses(million) LR/SR	Reported coverage % LR/SR	potency	Potency test applied Yes=1 No=0
1	670.000 570.000	purchased	-	90-100 58	>6PD50	0
2	14.700.000 38.500.000	producted	27.600.000 1.900.000*	91 97	>6PD50	1
3	97.300.000 95.700.000	both	4,185,300	3	Variable 3->6PD50 and unknown	0
4	2 087 563 4 567 112	both	706 291 1 052 924	33 23	unknown	0
5	2,750,000 8,800,000	purchased	2.700.000 1.600.000	100 37	>6PD50	1
6						

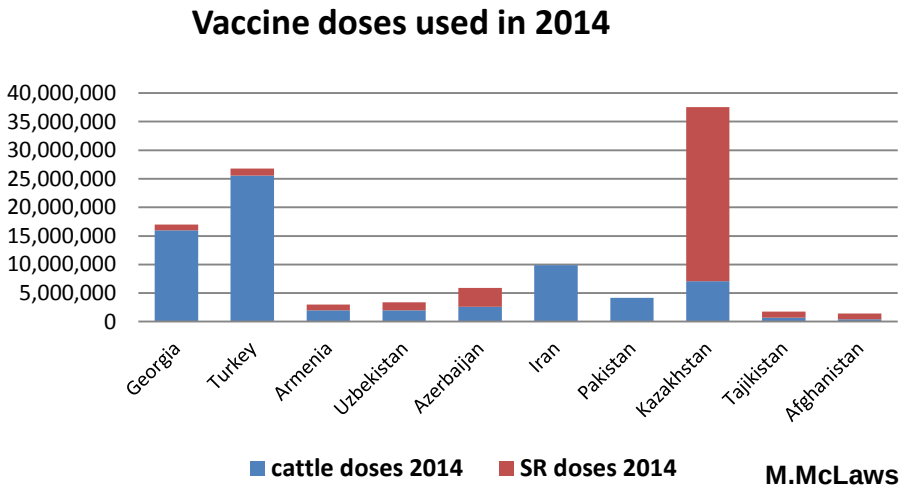
- Therefore, data was used that provided from checklist for each countries

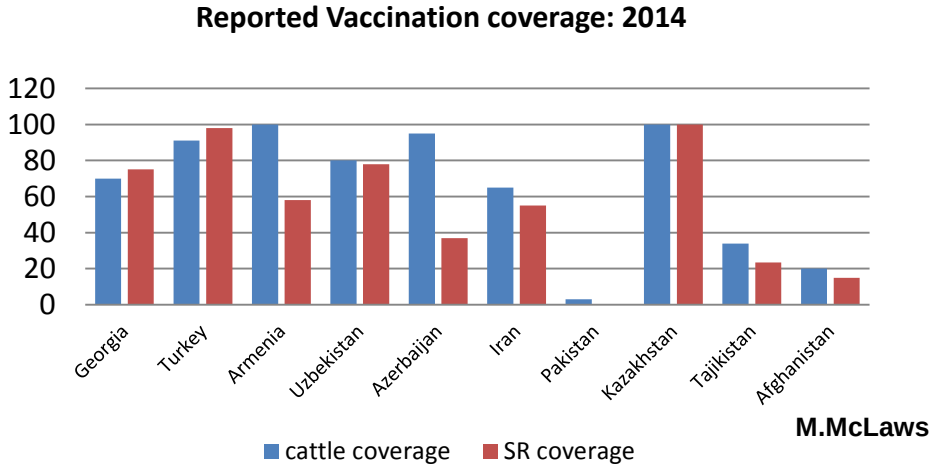
Summary

1. Vaccine doses used in 2014: 70m and 40m for LR and SR respectively (roughly in total/year)
2. Coverage is ranged from 3-100% for LR and 0-100% for SR

Doses used in region (without Russia): 2008: 92 mln.; 2010: 178 mln. For total 410 mln. FMD susceptible animals in region; ***2013 4thWE Ann.meeting by K.Sumption***

3. Although SR vaccination is not included into strategic vaccination campaign in some countries, there is a significant gap on between used vaccine and population size; particularly some endemic setting area







Conclusion

- There is a gap on between population existed in the region and vaccine available to use for vaccination to existed population
- Scientifically, high potency vaccine has significant advantages by supressing clinical disease as well as infection vs 3 PD50 vaccine.
- Authorities should consider that the results of homologous and heterologous challenge sometimes vary with the same strain, although used vaccine is high potency
- Mechanism and effort for increasing coverage of vaccination should be encouraged and supported
- Establishing board for vaccine marketing authorization is essential in order to ensure production of safe, efficient and potency vaccine appliance with international standards



Conclusion

- Disease managers should take account their own cost&benefit analysis and risk assessment for updating vaccination policy
- Since being gap on available vaccine to use, disease managers should consider that they give prioritization on immunize their population with optimal coverage level by vaccine with at least 3 PD50 vaccine, if not possible to use high potency vacc.; then try to enhance potency of used vaccine in endemic setting condition.
- It is clear that using high potency is the best option for elimination of virus circulation