Foot and Mouth Disease Vaccine Research and Development in India

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Foot and Mouth Disease in India
Present Status

- *Large Susceptible population*
- Disease endemic due to serotypes O, A & Asia1
- Increased vaccination coverage during last 5 years
- Reduction in disease incidence
- Still a long way to go
FMD Vaccine Production in India

- Early work started in Mukteswar 1960s – late 1970s
- 1972 – 79 Production facility established with govt aid from Denmark at Bangalore
- 1980 Vaccine production in fermentors commenced
- Simultaneously at BAIF Pune (Intervet)
- 1982 – Indian Immunologicals established
- Two more production facilities created recently (M/s Brilliant, M/s Biovet)
FMD Vaccine Production in India

- Total Capacity in the country at present about 350 Million trivalent
- Expected to reach about 600 million by 2015
- The vaccine is also exported to different countries
- More demand due to the regional initiatives in South Asia
- The capacity is expanded by different manufacturers & entry of new companies?
FMD Vaccine Production in India

• Uniformity in strains used for domestic use regulated by Govt
• Same technology followed for production of conventional vaccine
• Oil Adjuvanted vaccine widely used in all species
• Large volumes exported to other countries
Issues for FMD Vaccine Research

• Thermo stability of the vaccine
• Duration of immunity, effective and safe adjuvants
• Broad antigenic coverage for the emerging viral strains
• Ease of administration for mass coverage
• Cost effective scale up without dependence on expensive infrastructure
• DIVA enabled technology
• Common vaccine platform to accommodate newly emerging field strains to address region specific epidemiology.
Research on FMD vaccines

- At the Bangalore Campus R&D on FMD vaccine being carried out during last 3 decades
- Improvements to conventional vaccines
- Several approaches for new generation vaccines: expression of VP1, P1-2A, P1-2A-3C attempted in several platforms including bacteria, yeast
- Development of DNA vaccines & nanoparticle delivery
- Chimera using Asia1 infectious clone
Research on FMD vaccines

Current Vaccine Research initiatives at IVRI

1. Evaluation of FMD vaccine formulated with novel adjuvants
2. Development of adenovirus vector based FMD vaccine (USDA-IVRI-PDFMD)
3. Using baculovirus expressed capsid proteins as candidate vaccine
4. Developing stable vaccine virus for use with conventional vaccine (infectious cDNA approach)
Increasing duration of immunity of conventional vaccine

• Evaluation of high pay load vaccine using three adjuvants (A, B and C)
  – Pay load used O-14μg, type A-11μg and Asia1-14 μg
  – 2ml dose by intramuscular and subcutaneous
  – 8 animals per group (9 groups including control)
  – Humoral response by SNT at regular intervals till 9 months
  – Booster vaccination in three groups at 6 months

• Results based on SN Ab response are encouraging
• Booster dose induced a robust Ab responses in all groups.
• Study is being continued to determine the duration of immunity by SNT and challenge at 1 year.
• Additional studies for optimizing payloads planned
Evaluation of FMD vaccine formulated with novel adjuvants

![Graph showing Geometric Mean Titer (Log_{10} SN_{50}) over weeks post-vaccination for FMD type O (Unboosted) and FMD type O (Boosted).](image)
FMD Type O

Geometric Mean Titer (Log_{10} SN_{50})

Weeks Post-vaccination

Control
Adjuvant A
Adjuvant B
Adjuvant C

Booster
FMD Type A

Unboosted

Boosted

Geometric Mean Titer (Log_{10} SN_{50})

Weeks Post-vaccination

Control  | Adjuvant A | Adjuvant B | Adjuvant C

Control  | Adjuvant A | Adjuvant B | Adjuvant C

Booster
Geometric Mean Titer (Log_{10} SN_{50})

Weeks Post-vaccination

Control  Adjuvant A  Adjuvant B  Adjuvant C

Booster
FMD Type Asia-1

Unboosted

Boosted

Booster
FMD Type Asia-1

Geometric Mean Titer (Log$_{10}$ SN$_{50}$) vs. Weeks Post-vaccination

- Control
- Adjuvant A
- Adjuvant B
- Adjuvant C

Booster
Development of Novel FMD Vaccine: Empty Viral Capsids

- Novel subunit vaccine containing only FMDV genes coding for capsid antigens and viral nonstructural proteins
- Efficacy in rapid induction of protective immunity following a single shot of vaccine
- Allows easy differentiation of infected from vaccinated animals – DIVA
- Safe to produce since no infectious FMDV
- Deliver using replication-defective human adenovirus vector

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Adeno Vectored Vaccine

• Constructed recombinant hAd5 – FMDV for Indian vaccine strains (O,A & Asia1) and few candidate vaccine strains.

• Animal experiments to be done this year to study the response to mono/trivalent

• Duration of immunity & challenge studies in Cattle & buffaloes
Expression of empty Viral capsids of FMDV in insect cells

1. Expressed capsid proteins (P1-2A-3C) of FMDV type O, A and Asia 1

2. Studies on evaluating the baculo expressed capsid proteins as candidate vaccine antigens is in progress
Production of more potent, stable and safer vaccine is possible through genetic engineering of the infectious cDNA generated from the parental virus.

**Progress**

Infectious clones of FMDV-type O and Asia 1 developed.

Further work on producing viruses with improved capsid stability is in progress.
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