FREEZING OF FORMULATED FMDV VACCINES AND VACCINE BANKS: POTENTIAL FOR A FASTER RESPONSE IN EMERGENCY SITUATIONS

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Freezing and storage of formulated FMD vaccines at -20°C

1. Introduction and rationale
2. Effect on emulsion quality and microscopic appearance
3. Immediate effect on immunogenicity or potency
4. Prolonged effect on immunogenicity and stability

SPC: DO NOT FREEZE

W/O/W emulsions (Montanide ISA 206) or W/O emulsions should not be frozen (SEPPIC, France)

Oil adjuvanted vaccines stored at -20°C or -70°C show reduction in potency (Barnett PV Vaccine 20, (2002) 2060-2064)

Montanide ISA 206 can be snap frozen and kept at ultra low temperature (SACS vaccine concept) without detrimental effect on potency (Barnett PV Vaccine 20, (2002) 2060-2064)

Antigen and vaccine banks

Time and fast response are of crucial importance in case of an FMD outbreak.

Antigen banks (-196°C) require immediate formulation (3-5 days) in case of an outbreak. Logistic challenge (minimal batch size, transport) and no final release testing (safety and potency) possible.

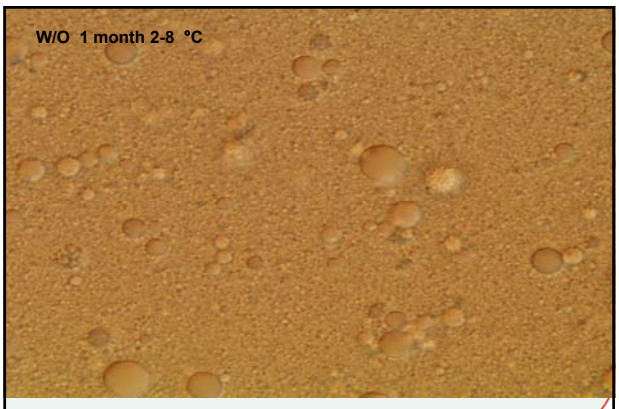
Vaccine banks (4°C) subject to declining stability of FMDV require frequent replenishment by fresh vaccine stocks.

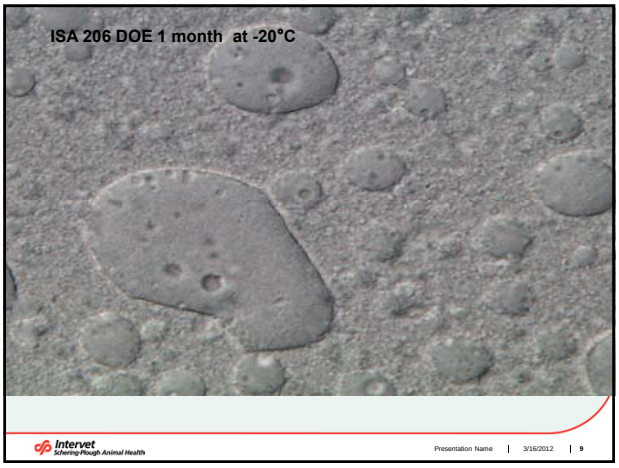
Despite the potentially much faster response of ready-to-use vaccine banks they are relatively costly and therefore compared to antigen banks their use currently is relatively limited.

Effect on emulsion quality, microscopic appearance and potency of -≤20°C freezing:

- Trivalent vaccines (O1Manisa, A Tur 20/06, Asia 1 Shamir)
- Standard antigen production, formulated at regular payloads
- Formulated with different adjuvants (Montanide ISA 206 and 2 types of W/O)
- 1 vial kept at 4°C, 1 vial frozen at -20°C using a regular compressor type house-hold freezer.
- Kept frozen at -20°C for 1 month
- I.M. vaccination in guinea pigs (n=6/group), serology 3 weeks after vaccination by VNT titres

W/O 1 month 2-8 °C





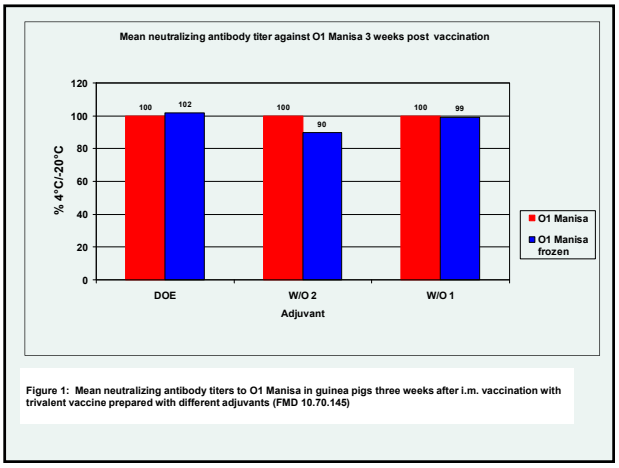


Figure 1: Mean neutralizing antibody titers to O1 Manisa in guinea pigs three weeks after i.m. vaccination with trivalent vaccine prepared with different adjuvants (FMD 10.70.145)

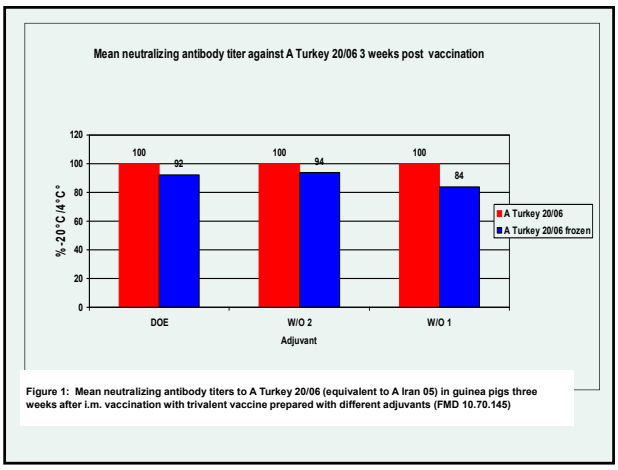


Figure 1: Mean neutralizing antibody titers to A Turkey 20/06 (equivalent to A Iran 05) in guinea pigs three weeks after i.m. vaccination with trivalent vaccine prepared with different adjuvants (FMD 10.70.145)

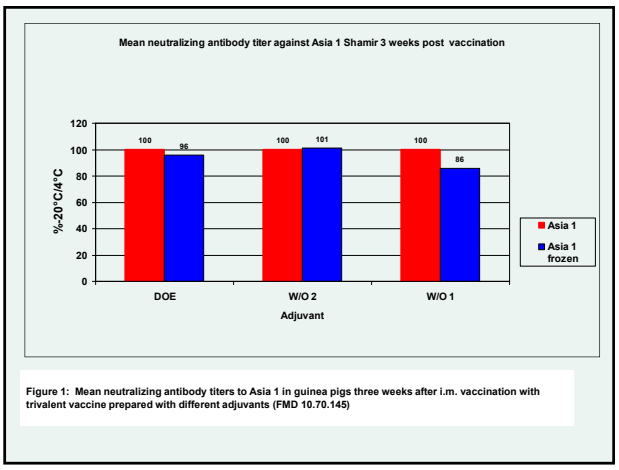


Figure 1: Mean neutralizing antibody titers to Asia 1 in guinea pigs three weeks after i.m. vaccination with trivalent vaccine prepared with different adjuvants (FMD 10.70.145)

Effect on stability: Materials and methods

- Monovalent, Bivalent and Trivalent vaccines (O1Manisa, A Tur 20/06, Asia 1 Shamir)
- Formulated with Montanide ISA 206
- 1 vial kept at 2-8°C, 1 vial frozen and kept at -20°C.
- Kept frozen at -20°C using a regular compressor type house-hold freezer for a period of **16 months**
- I.M. vaccination in guinea pigs (n=6/group), serology 4 weeks after vaccination by VNT titres
- 1 frozen trivalent vaccine containing (O1Manisa, A22 Iraq, Asia 1 Shamir) kept for a period of **41 months** and tested in guinea pigs.
- 1 frozen trivalent vaccine containing (O1Manisa, A22 Iraq, Asia 1 Shamir) kept for a period of **14 months** and tested in cattle

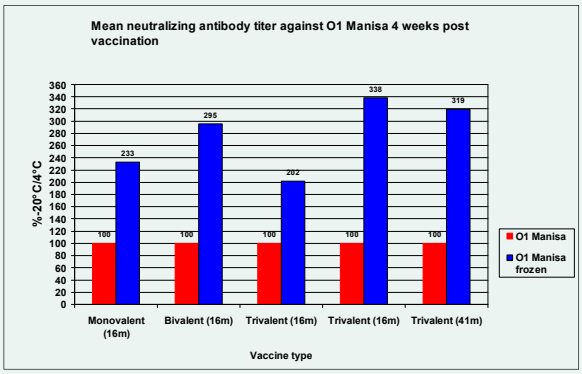


Figure 1: Mean neutralizing antibody titers to O1 Manisa in guinea pigs four weeks after i.m. vaccination (FMD 10.70.146)

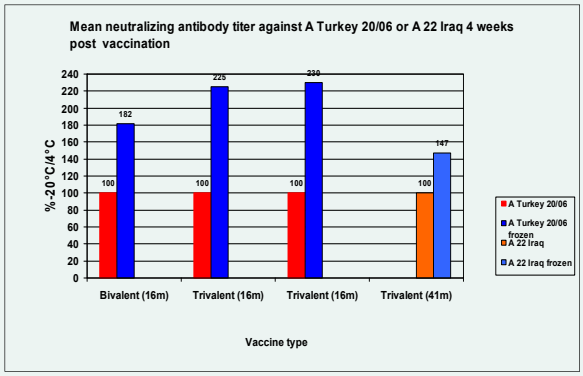


Figure 2: Mean neutralizing antibody titers to A Turkey 20/06 (equivalent to A Iran 05) or A 22 Iraq in guinea pigs four weeks after i.m. vaccination (FMD 10.70.146)

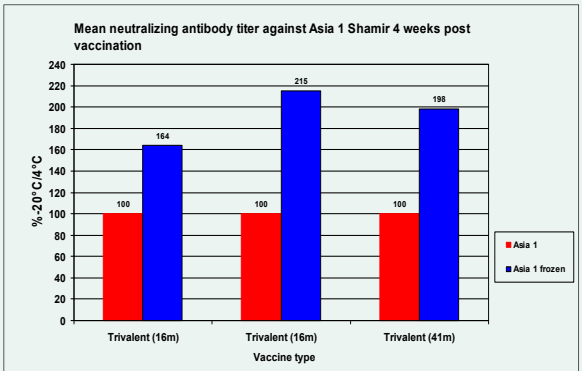


Figure 3: Mean neutralizing antibody titers to Asia 1 Shamir in guinea pigs four weeks after i.m. vaccination (FMD 10.70.146)

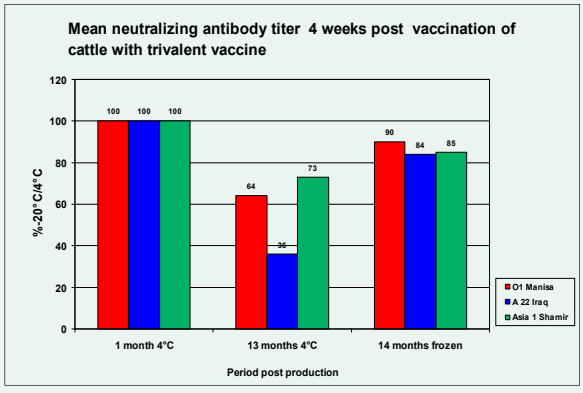


Figure 4: Mean neutralizing antibody titers in cattle four weeks after i.m. vaccination (FMC 07.70.000D, FMD 08.70.034, FMD 08.70.039)

Conclusions

1. In contrast to general prescriptions and perception, freezing of oil adjuvanted FMD vaccine is not necessarily detrimental to vaccine quality.
2. Although a (minimal) negative effect on the microscopic appearance of the emulsion can be observed, DOE and SOE formulated FMDV vaccines can be frozen at -20°C without an immediate negative effect on the potency of the vaccine and more importantly with improved shelf-life.
3. Freezing of ready to use FMDV vaccine greatly enhances the possibilities and use of vaccine banks like:
   - Frozen vaccine can be stored in the country of destination and at any quantity.
   - Vaccine is ready for immediate use, allowing for a faster response and emergency vaccination in case of an outbreak.
   - No "stand by" formulation production facilities needed, no minimum batch size.
   - Vaccine batches from the bank can be tested for vaccine and safety before release.