



# Role of manufacturers for a timely supply of affordable and fit-for-purpose vaccines

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**1**  
GENERAL  
PRINCIPLES

**2**  
EPIDEMIO-  
LOGICALLY  
RELEVANT  
STRAINS

**3**  
"IMMUNO-  
DOMINANT"  
STRAINS

**4**  
ADEQUATE  
POTENCY

**5**  
NSPs &  
DIVA

**6**  
COST-  
EFFECTIVENESS





# GENERAL PRINCIPLES



- FMD CONTROL PROGRAMS
- VACCINE PRODUCTION



# FMD Control Programs

**Vaccination** is recognized as an important tool in **Foot-and-Mouth Disease (FMD) control**.

The role of **Manufacturers** for a **timely** supply of **affordable** and **fit-for-purpose** vaccines in **all** regions of the world is therefore pivotal.



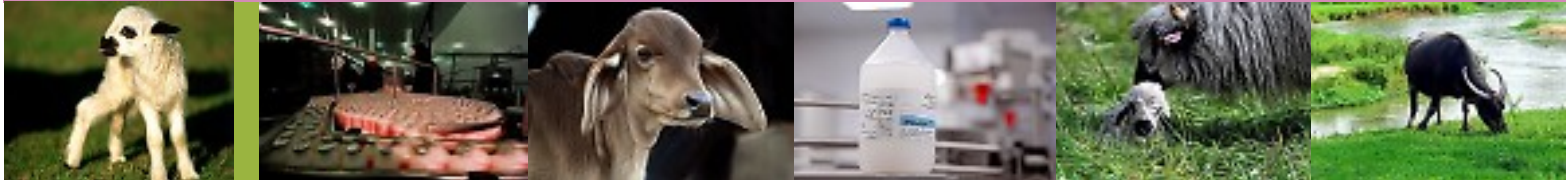
# FMD Vaccine Production

The production of such vaccines requires a profound **scientific** and **technical** knowledge and extensive **experience** in a number of fields:

- The Manufacturers must follow internationally accepted principles of **Quality Assurance** and **Good Manufacturing Practice** as a minimum prerequisite.
- They must also know how to **select** and **adapt** new vaccine strains, how to **cost-effectively** make vaccines out of them, at the required level of **potency** and **purity**.



# EPIDEMIOLOGICALLY RELEVANT STRAINS



- EPIDEMIOLOGICAL VIGILANCE
- DEVELOPMENT OF NEW VACCINE STRAINS
- $r_1$  VALUE AS A TOOL FOR MONITORING FIELD STRAINS



# EPIDEMIOLOGICAL VIGILANCE

The use of the most appropriate vaccine as part of an integrated control program relies on an in-depth knowledge of the **virus strains circulating** in the **region**.

In that respect, OIE Regional Reference Laboratories play a significant role in **collecting** and **studying** field isolates, then **publishing** the epidemiological characteristics of these strains and **making them available** to manufacturers.



# DEVELOPMENT OF NEW VACCINE STRAINS

Collection of Field  
Samples by Vet.  
Authorities



Reference  
Laboratory



Identification  
& Official  
Designation  
of Isolate



Official  
Request  
for Sample



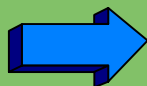
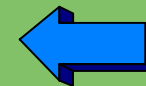
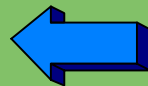
## TESTING & ADAPTATION

### Production Unit

1. Production Yield
2. Replication Rate
3. Stability
4. Inactivation Data
5. Documentation

### QC Laboratory

1. Cross Serology with Vaccine Strains by VNT
2. Replication rate in production and test cells
3. Documentation



**FINAL PRODUCT CRITERIA**  
Antigenic Load & Potency



# r1 VALUE AS A TOOL FOR MONITORING FIELD STRAINS (1/2)

Results of heterologous intra-serotypic serological tests (“r1 values”) have been extensively used for the evaluation of the **expected heterologous protection** against the current field isolates.

For that purpose, responsible manufacturers are expected to generate sets of **antisera** corresponding to their vaccine strains.

They also **monitor** these **field strains** regularly to assure that their vaccine strains (as well as the content of their antigen banks) remain up to date.



# r1 VALUE AS A TOOL FOR MONITORING FIELD STRAINS (2/2)

Whenever a field strain with significantly low\* r1 value against the vaccine strain **sustainably** circulates in the field, manufacturers should start the adaptation of this new strain, unless indicated otherwise by heterologous challenge studies (vaccine coverage might be **broadened** by using **high potency vaccine**, Brehm et al., 2008).

In an **endemic** situation, where large quantities of the same vaccine are routinely employed, there is clearly a significant value in matching the vaccine strain(s) to the field viruses **as exactly as possible** so that the vaccine program is optimized.

\* (< 0.3 by Virus Neutralization Test according to IAH)



# « IMMUNODOMINANT » STRAINS



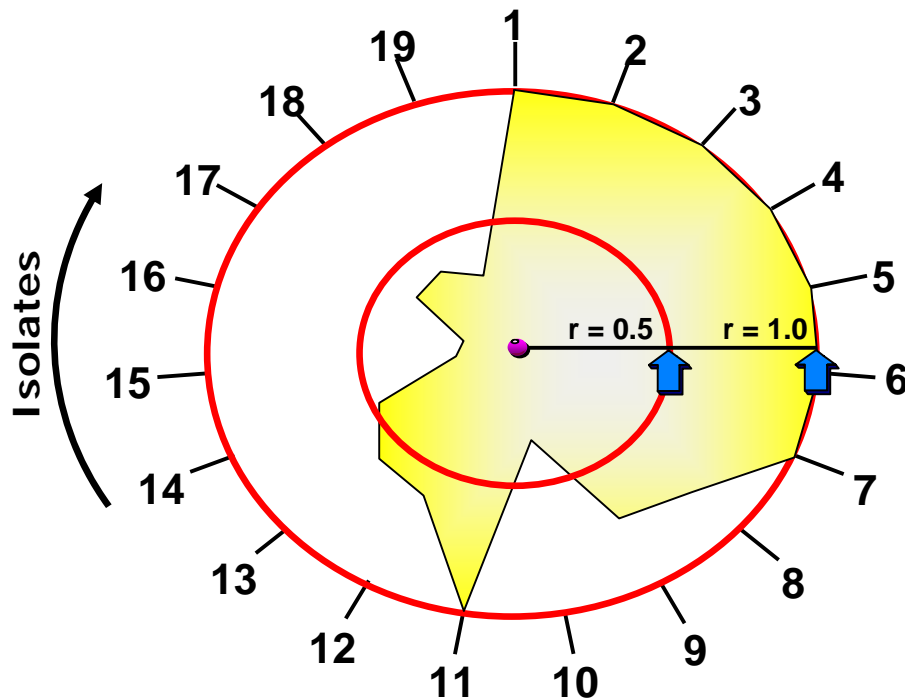
- WHAT IS AN « IMMUNODOMINANT » STRAIN?
- PRACTICAL CONSEQUENCES

# WHAT IS AN "IMMUNODOMINANT" STRAIN?

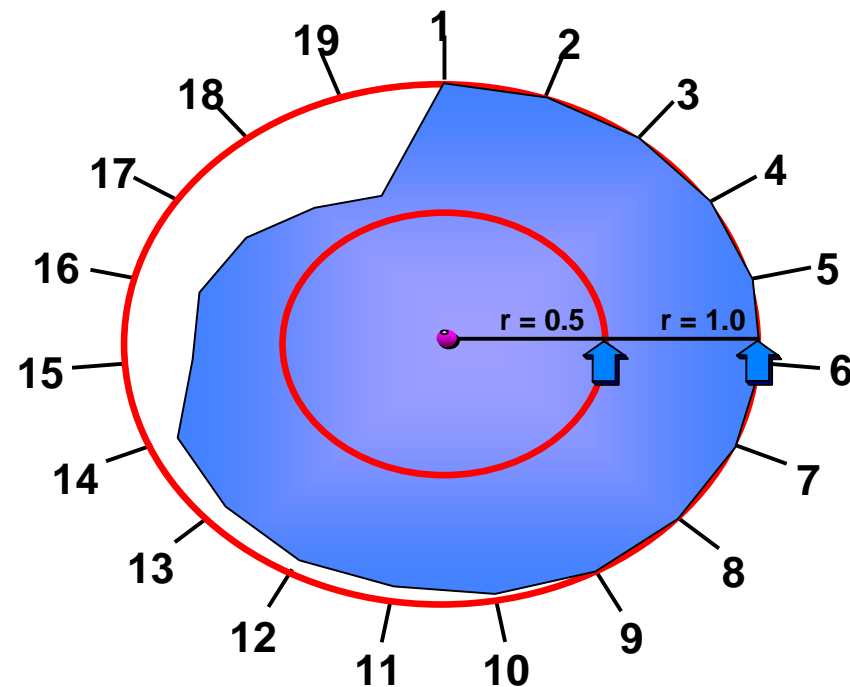
A more immunogenic strain with a broader cross-reactivity

Relative Reactivity of Vaccinated Cattle Sera with 19 Field Isolates from Saudi Arabia (Doel et al, 1995). Expressed as 'r1' Values.

O Manisa Vaccine Sera



O 3039 Vaccine Sera



If  $r = 1$  then there is 100% homology between vaccine strain and field strain.  
 O 3039 Vaccine matches all field strains significantly better or equal to O Manisa Vaccine.

## PRACTICAL CONSEQUENCES

- Beyond the need to match field and vaccine strains, the selection of “**immunodominant**” strains is of considerable importance, especially in the currently fast changing epidemiological environment of the Near and Middle-East.
- Most current vaccine strains older than 20 years have retained their value due to this characteristic.
- In our hands, and as demonstrated by IAH-Pirbright with recent field isolates, **Asia1 Shamir** is also an “immunodominant” strain which, with the relatively low level of antigenic variation seen with this serotype, makes it an exceedingly valuable virus.
- Clearly, the **isolate(s) chosen** by different manufacturers to adapt to tissue culture and the **methodology** used in the adaptation could result in fundamentally **different vaccine strains bearing the same generic name**.
- Of course, the probability of finding an “immunodominant” strain is directly proportional to the effort invested.



## ADEQUATE POTENCY & TIMELY DELIVERY



- « HIGH » POTENCY VERSUS « REGULAR » POTENCY
- TIMELY DELIVERY

## "HIGH" VERSUS "REGULAR" POTENCY

"HIGH" (>6 PD50) Potency vaccine have been proven to **protect cattle as early as four days post-vaccination** when tested by contact challenge.

They are particularly useful in **emergency situations** when vaccines are finished from antigens held in a bank and injected to naive animals.

"REGULAR" (>3 PD50) Potency vaccine are recognized as **fit-for-purpose** when consistently used in **endemic settings** in view of controlling **clinical disease**.

# TIMELY DELIVERY



The cryostorage of concentrated, purified FMD antigens offers many advantages in relation to **emergency vaccine usage in regions free of FMDV**, but also for **endemic regions**:

- Long term **stability** of antigen
- Only used **if needed**
- Vaccine **rapidly** made

**Flexibility** to formulate according to the circumstances notably:

- Potency
- Dose volume
- Adjuvant
- Valency
- Packaging
- Batch size



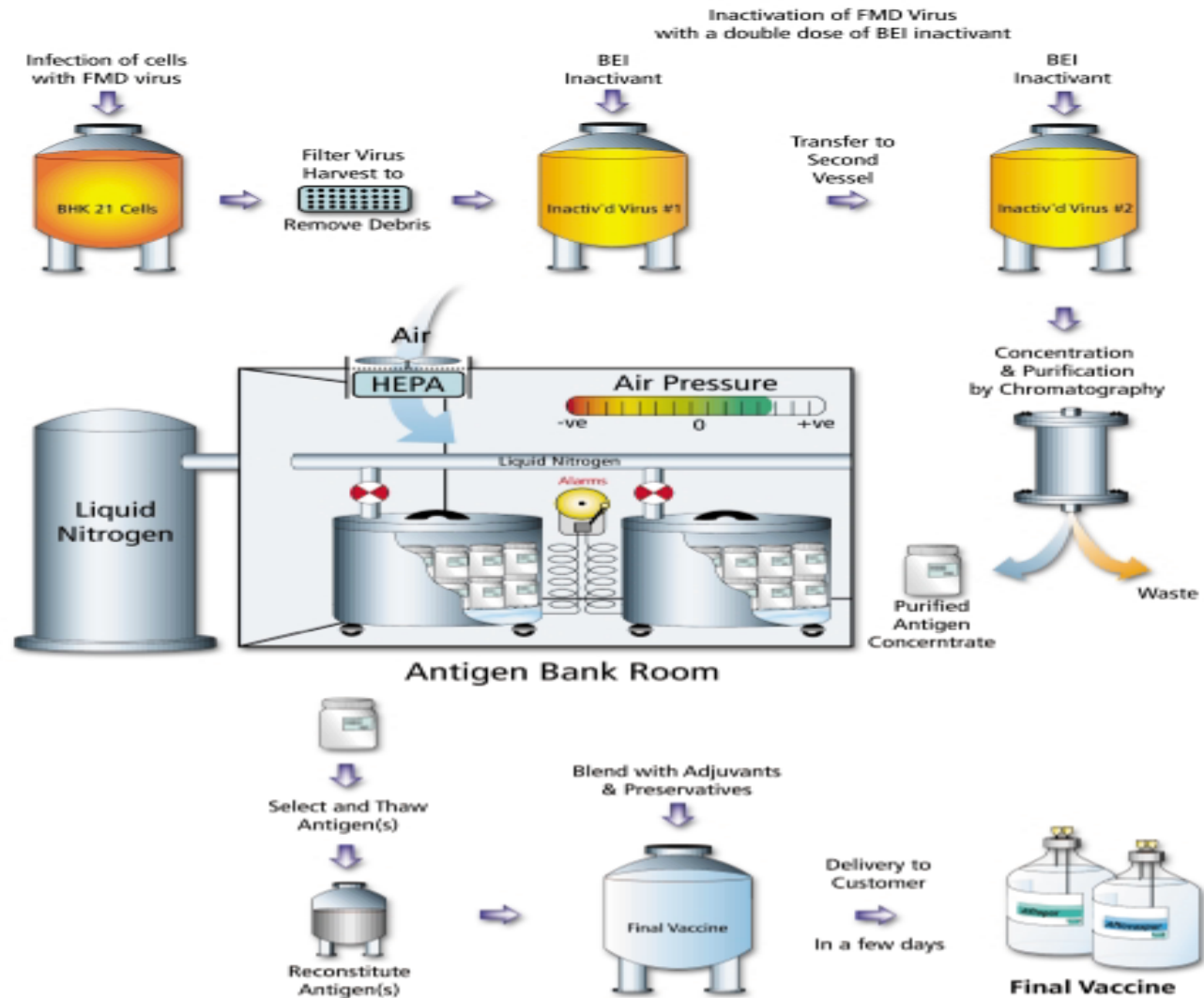
## NSPs & DIVA



- PURIFICATION OF ANTIGENS AT INDUSTRIAL SCALE
- NSPs and « DIVA » VACCINES



# PURIFICATION OF ANTIGENS AT INDUSTRIAL SCALE



# NSPs AND “DIVA” VACCINE

Validated processes of purification of antigens remove most of FMDV Non Structural Proteins (NSPs), the marker of FMDV infection.

Consequently, vaccines produced from such purified antigens have the valuable property **not to interfere with serological surveys** carried out to identify **infected/carrier** groups of animals in the vaccinated population.



# COST EFFECTIVENESS



- TECHNOLOGY AND CAPACITY OPTIMIZATION
- TECHNOLOGY TRANSFER



## TECHNOLOGY AND CAPACITY OPTIMIZATION

Cost effectiveness is achieved through harnessing the technology and optimizing the capacity of vaccine Manufacturing plants.



# TRANSFER OF TECHNOLOGY

Cost effectiveness can also be achieved through transferring technology locally whenever the option is proven viable, e.g.:



The collaboration between the **Botswana Vaccine Institute** and **Meril** started in 1978...

... and is continuing in 2009 with the construction of a new manufacturing building.



## IN CONCLUSION...

As described, manufacturers already play a significant role in a number of fields related to technical and economical improvement of FMD vaccines.

However, in order to harness novel technologies, develop more targeted products and supply cost-effective vaccines, public institutions and industry should continue to:

- direct their research efforts in vaccine development and,
- collaborate wherever possible to achieve these objectives.





# Thank you for your attention

