PANAFTOSA

PAN-AMERICAN HEALTH ORGANIZATION
WORLD HEALTH ORGANIZATION

THE USE OF DIAGNOSTIC NCP KITS/TESTS FOR FOOT-AND-MOUTH DISEASE IN CATTLE AND OTHER SUSCEPTIBLE SPECIES: CONSTRAINTS AND CHALLENGES

Features of FMD-NCP Testing

Identify infection:

- Irrespective of vaccination status
- Independent of serotype/subtype

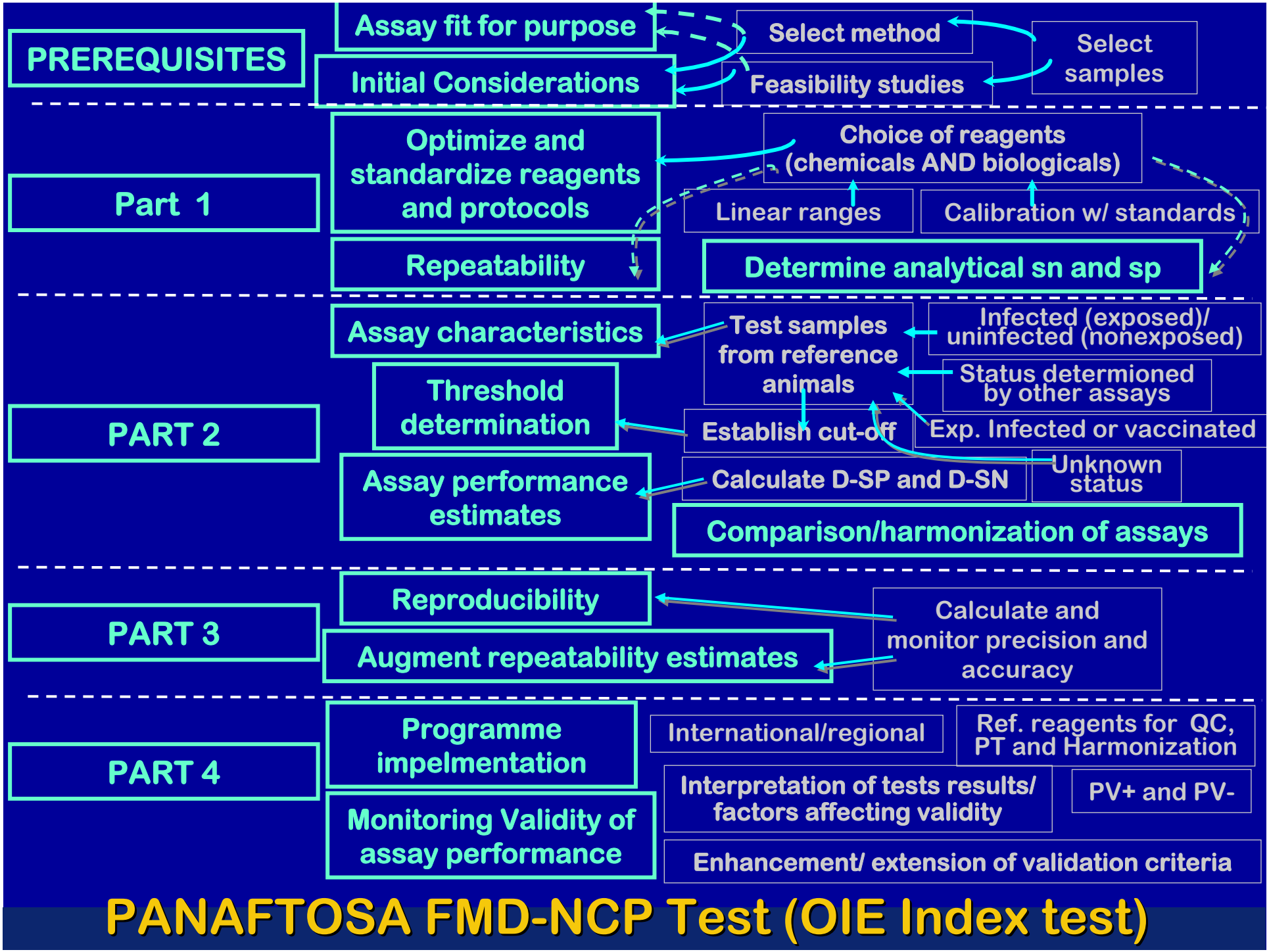
Impact

- Recognition of free areas with vaccination
- Vaccination to live policy

Main aims of FMD-NCP Testing

- Substantiate absence of viral activity
- Post-outbreak serosurveillance

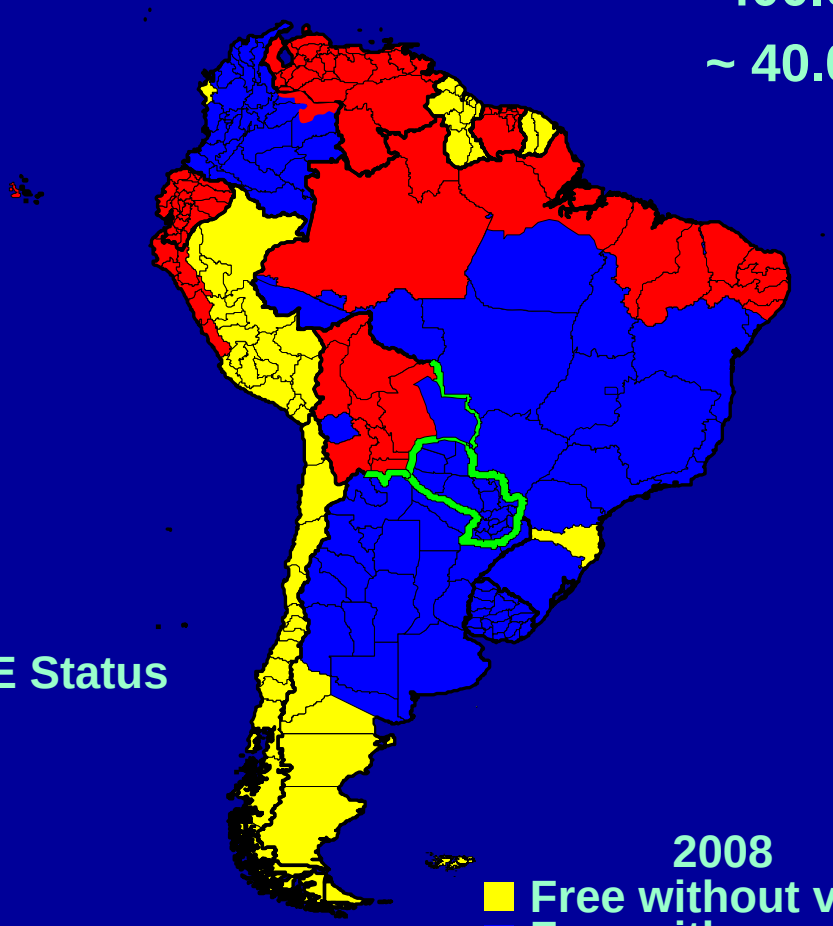
- Outbreak confirmation
- Input for Import / Export
- Outbreak alert
- Estimate prevalence of infection
- Screening infection prior to evaluation of population immunity


PREREQUISITES
Assay fit for purpose
Initial Considerations
Select method
Feasibility studies
Select samples
Part 1
Optimize and standardize reagents and protocols
Repeatability
Choice of reagents (chemicals AND biologicals)
Linear ranges
Calibration w/ standards
Determine analytical sn and sp
PART 2
Assay characteristics
Threshold determination
Assay performance estimates
Test samples from reference animals
Infected (exposed)/ uninfected (nonexposed)
Status determioned by other assays
Establish cut-off
Exp. Infected or vaccinated
Calculate D-SP and D-SN
Unknown status
Comparison/harmonization of assays
PART 3
Reproducibility
Augment repeatability estimates
Calculate and monitor precision and accuracy
PART 4
Programme impelmentation
Monitoring Validity of assay performance
International/regional
Ref. reagents for QC, PT and Harmonization
Interpretation of tests results/ factors affecting validity
PV+ and PV-
Enhancement/ extension of validation criteria
PANAFTOSA FMD-NCP Test (OIE Index test)

WIDE USE FOR RECOGNITION OF FMD-FREE AREAS BY OIE

~ 400.000 screening tests/year

~ 40.000 confirmatory tests/year



FMD OIE Status

2008

- Free without vaccination
- Free with vaccination
- Not Free (50 x 10^6)
- High Surveillance Zone

- Other regions
- New kits/ “in house” tests/new developments

Challenge

Equivalence of results/interpretations and maintenance of performance characteristics of kits including the index test

EQUIVALENCE OF TESTS' RESULTS

1- VALIDATION (complete, upon OIE guidelines)

2 – VERIFICATION TESTING AND COMPARATIVE EXERCISES

3 – ADEQUATE PANELS

4 – FOLLOW-UP (maintenance of performance characteristics)

5 – INTERPRETATION OF RESULTS (FACTORS AFFECTING VALIDITY)

6 – APPROPRIATE USE

VALIDATION

	Kit A
CLAIMED (DSn)	94%
Non Vacc. + Infected* > 28 dpi	93%
Vacc + Inf. > 28 dpi	60%

*Experimental or natural infection

- LIMITED AND FRAGMENTED DATA

- OTHER PROBLEMS:
  - LIMITED INFORMATION OF FIELD DATA TO SUBSTANTIATE FINDINGS;
  - POORLY PLANNED VALIDATION EXERCISES;
  - LIMITED QUALITY CONTROLS IN TEST KITS;
  - LIMITED REFERENCE MATERIAL FOR LIVESTOCK POPULATIONS, PARTICULARLY COVERING THE WHOLE SPECTRUM OF FMD INFECTION/VACCINATION SCENARIOS;
  - CLAIMS OF TEST PERFORMANCE THAT CANNOT BE SUBSTANTIATED

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VERIFICATION TESTING AND COMPARATIVE EXERCISES

Testing performed previously have pointed out:

- Need to perform periodic assessments (eg. some kits changed the formats)
- Multi-laboratory projects (avoid conflicts of interests)
- The role of OIE reference laboratories
- Importance of using adequate panels
- Need for guidelines

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ADEQUATE PANELS

- Availability for adequate standards and panels (constitution, number and volume of sera, broad range of reactivity, satisfactory stability, and the capacity to discriminate performance sensitivity)

- OIE guidelines

- Cattle:

  Stong+, Weak+, and Negative Standard Sera

  2 evaluation panels (different composition)

- Other hosts:

  no standards or panels available

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FOLLOW UP

Need to monitor maintenance of kits/tests performance characteristics

- Batch control (Producer/External)
- Periodic monitoring of reproducibility between laboratories

FOLLOW UP (cont…)

Batch control

Considerable differences in performance among batches have been observed for some companies

Certificate of Analysis

Batch Control: Producer

Need of unified criteria for information to be included in the CA (available to official control)

Performance			
Specificity	16 sera	Not included	183 sera
Sensitivity	Not included	Not included	68 sera
Grey zone (panel sera)	Not included	Not included	70 sera
Performance of reference panel	5 sera	Not included	16 sera

* Total number of determinations not informed

** At least 12 determinations in 5 different tests

*** No information on reactivity values (strong or weak positive sera???)

**** Informed for control sera (positive and cut-off serum)

Batch control

Official control:
- CAs from manufacturers
- Eventual confirmatory testing
- Retention of batch samples should problems arise

User feedback
IQC: Charts

– constant record
– interplate repeatability (daily, monthly and tearly basis)
– identification of unacceptable results
– recognition of reagent problems
– trends in results (increasingly poor performance)
– identify operator differences
– GLP
– external recognition

FOLLOW UP (cont…)

Periodic monitoring of reproducibility between laboratories

HOW????

- Ad Hoc/Consortium?????
- Proficiency Testing???

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INTERPRETATION OF RESULTS (FACTORS AFFECTING VALIDITY)

TEST RESULTS ARE USEFUL ONLY IF THE INFERENCES MADE ARE ACCURATE

- Guarantee absence of vaccine interference
- PV+ and PV- (survey design)
- Minimum requirements and definition of testing algorithms for different purposes

INTERPRETATION OF RESULTS (FACTORS AFFECTING VALIDITY)

Guarantee absence of vaccine interference

✓ OIE established procedures for registration and for batch control

✓ Most countries in SA have implemented procedures to monitor absence of vaccine interference

✓ Approach based on forcing an immune response upon revaccination

Other hosts?????? Other regions??????

INTERPRETATION OF RESULTS (FACTORS AFFECTING VALIDITY)

PV+ and PV- (survey design)

Impact of prevalence on the predictive value

Prevalence (%)	.1	1.0	2.0	5.0	50.0
PrV + (%)	1.9	16.9	27.9	50.5	95.0

DSn and DSp = 95%

		Animals TP	TN	
TEST	+	95	4995	5090
	-	5	94.905	94.910
		100	99.900	100.000

$$\frac{TP}{P+} = \frac{95}{5090} = 1.86$$

INTERPRETATION OF RESULTS (FACTORS AFFECTING VALIDITY)

Minimum requirements and definition of testing algorithms for different purposes

- Screening + confirmatory
- Other formats

Needs further discussions (minimum DSn???)

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APPROPRIATE USE

Proficiency testing

- OIE guidelines

- Regional experience:
At least 5 rounds of PT performed (most laboratories participate)

- Need to revise:
Definition of Scope PT
Evaluation of adequate sera (number, characteristics, etc)
Assessment of the grey zone
Criteria for laboratory approval
Who should be responsible of performing PT (conflict of interest)

RESPONSABILITIES

Producer

- Supply robust, rugged, kits fit for use
- Produce good protocols and control standards
- Provide help desk services

Users

- Internal quality control
- Training
- Feedback

National organisations

- Train staff
- Monitor laboratory (EQA)
- Adopt standards
- Plan with knowledge of tests (surveys)
- Accreditation pathway

Regional/International organisations

- Standardise (standards set and adopted)
- Harmonisation exercises (proficiency testing, ring-tests, etc.)
- Collate and report results (epidemiology)
- Funding

CONSORTIUM / NETWORK / ?????
(OIE/FAO)

- ✓DEVELOP AND HARMONIZE PANELS
- ✓ ELABORATE RECOMMENDATIONS FOR:
  - PT (ORGANIZE???)
  - CA
- ✓ GATHER INFORMATION
- ✓ PROMOTE REASERCH PROJECTS
- ✓SEEK FINANCIAL SUPPORT

Pan-American Health Organization

Regional Office of the World Health Organization

Pan-American Foot and Mouth Disease Center
PANAFTOSA - PAHO/WHO

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