Challenges to control RVF disease: Research required to develop new diagnostic tools

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Outline

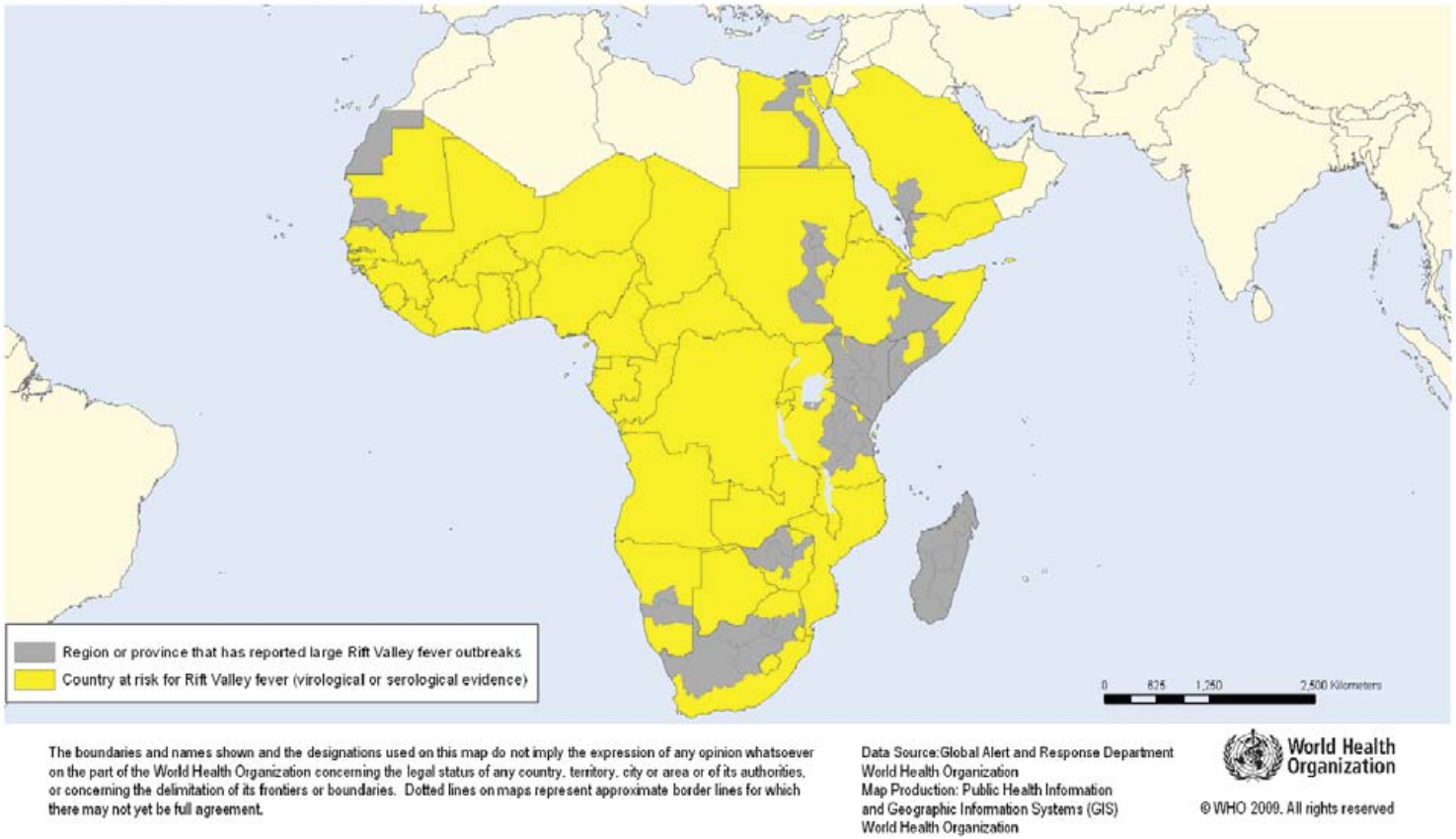
- Impact and importance of RVF
  - Animal health and trade
  - Human Health
- Laboratory Diagnostic of RVF
  - Current available tools
  - Opportunities for the development of new tools
- AU-PANVAC activities to support Animal Diseases diagnostic
- Conclusion

Impact and importance of RVF

- **Animal Health and Trade**
  - Zoonotic insect-borne viral disease caused by a Phlebovirus.
  - It can cause abortion & mortality.
  - Primarily affects ruminants, but also has the capacity to infect humans & many other species.
  - Irregular occurrence (every 5-7 years) reliant on the presence of susceptible animals, build-up of the mosquito vector population and the presence of the virus.

Impact and importance of RVF

- **Animal Health and Trade…**
  - Localised in Africa, RVF spread to the Middle-East (Saudia Arabia & Yemen) in 2000



Geographic distribution of RVF outbreaks in animals and humans, 1997–2010 (Source: World Health Organization)

Impact and importance of RVF

- **Animal Health and Trade…**

  - 1997/1998: Outbreak in Kenya and Somalia caused ban of livestock imports to the Middle-East from East Africa,

    - Affected Livestock export trade in the region particularly in Somalia

    - In 1997, year before the ban, **2.8 million live small ruminants** were exported from the port of Berbera (Somaliland region)

    - Losses due to the ban from Feb.1998 to May1999 were estimated at **$109 million** for the region of Somaliland alone.

Impact and importance of RVF

- **Impact on Human health:** Zoonotic disease

Outbreak dates	Geographic distribution	No. deaths confirmed
Dec 1997– Jan 1998	Kenya, Somalia, Tanzania	478 - -
Sep–Dec 1998	Mauritania	6
Aug–2001 Sep 2000	Saudi Arabia, Yemen	123
Nov 2006– March 2007	Kenya, Somalia, Tanzania	158 51 109
Sep 2007– Jan 2008	Sudan	230
Jan 2008– May 2009	Madagascar	26
Feb 2010– May 2010	South Africa	26
Sep 2010– Dec 2010	Mauritania	13

(Osman Dar et al., Emerging Inf. Dis. • Vol. 19, No. 2, Feb. 2013)

Laboratory Diagnostic of RVF

- **Available tools:** Common tests described in the OIE Manual of Diagnostic Tests and Vaccines (Chap 2.1.14)
  - **Identification of RVF virus:** early stage of infection

- Virus isolation using **cells lines** (Vero, BHK, CER-Chicken Embryo Reticulum) & **primary kidney or testis cells** (calves/lambs)

Laboratory Diagnostic of RVF

- **Available tools…**
  - **Identification of the agent …**
    - IFA on smears of liver, spleen and brain
    - Molecular Techniques: several technique available
      - ✓ Conventional PCR: based on NSs (***Garcia S., et al. 2001***), One step RT-PCR amplicon, 298 bp
      - ✓ Real time PCR
        - Protocol SYBER GREEN: based on L-GENE (***Bird et al.2007 and Labeaud et al., 2011***), Amplicon size 90 bp & specific dissociation peak is at 80°C
        - Protocol TAQMAN: ***Drosten et al., 2002***.
    - ELISA for Antigen detection
      - ✓ Immuno-Capture/sandwich ELISA

Laboratory Diagnostic of RVF

- **Current available tools…**
  - **Specific antibody (Ab) detection**
    - Kinetics of IgM (early antibodies) and IgG (later and persistent antibodies) directed against RVF virus

    - Ab detection used for RVF surveillance & Early warning: **IgM signs infection or vaccination**

Laboratory Diagnostic of RVF

- **Current available tools…**
  - **Specific antibody detection…**
    - Virus neutralisation tests (VNT)
      - ✓ Most specific diagnostic serological tests but require appropriate biosecurity facilities and qualified personel.
    - ELISA techniques: most widely used to detect IgM and IgG directed against RVF virus
      - ✓ Commercial ELISA Kits available
        - Capture ELISA: IgM & IgG ELISA Kits
        - iELISA (use recomb. Ag)
        - cELISA (no anti-species problems)

Laboratory Diagnostic of RVF

- **Opportunities for the development of new tools:**
  - **The new tools should facilitate livestock trade: 2 main research fields**

    1. Field tests: pen-side rapid assay

    - No commercial rapid "pen-side" available
    - Such test would be useful for early detection of the disease at the field level (rural disease)
    - Research on Pen-side test are underway for:
      - ✓ Antibodies detection: supported by GALVmed
        - based on RVF virus nucleoprotein for detection of antibodies in blood samples
      - ✓ Pen-side test for Antigens detection
        - Need to be encouraged

Laboratory Diagnostic of RVF

- **Opportunities for the development of new tools…**

2. Diagnostic tests for DIVA (Differentiate Infected & Vaccinated Animals) control strategy

- Several teams are working on DIVA tests approach
- Candidate Antigen: RFV virus Non-Structural Protein NSs (which is involved in the virulence)
  - ✓ **Publication 1**: *McElroy et al. (2009), Virology Journal, 6:125*
    - Deleted RVF virus-ΔNSs and companions tests (ELISA used as antigen NSs protein)
    - Antibody response in rats show that ELISA can distinguish animals infected with RVFV (wt) from those vaccinated with a ΔNSs virus

Laboratory Diagnostic of RVF

❖ **Diagnostic tests for DIVA (Differentiate Infected & Vaccinated Animals) control strategy…**

✓ **Publication 2**: *Fernandez et al., (2012), Clinical and Vaccine Immunology Vol. 19, p. 5–10*

- Sera from animals naturally infected by RVFV shown NSs antibodies

➢ Conclusion:

✓ ELISA using NSs protein as antigen is discussed as possible companions DIVA tests associate with the use of deleted ΔNSs-RVF virus as vaccine.

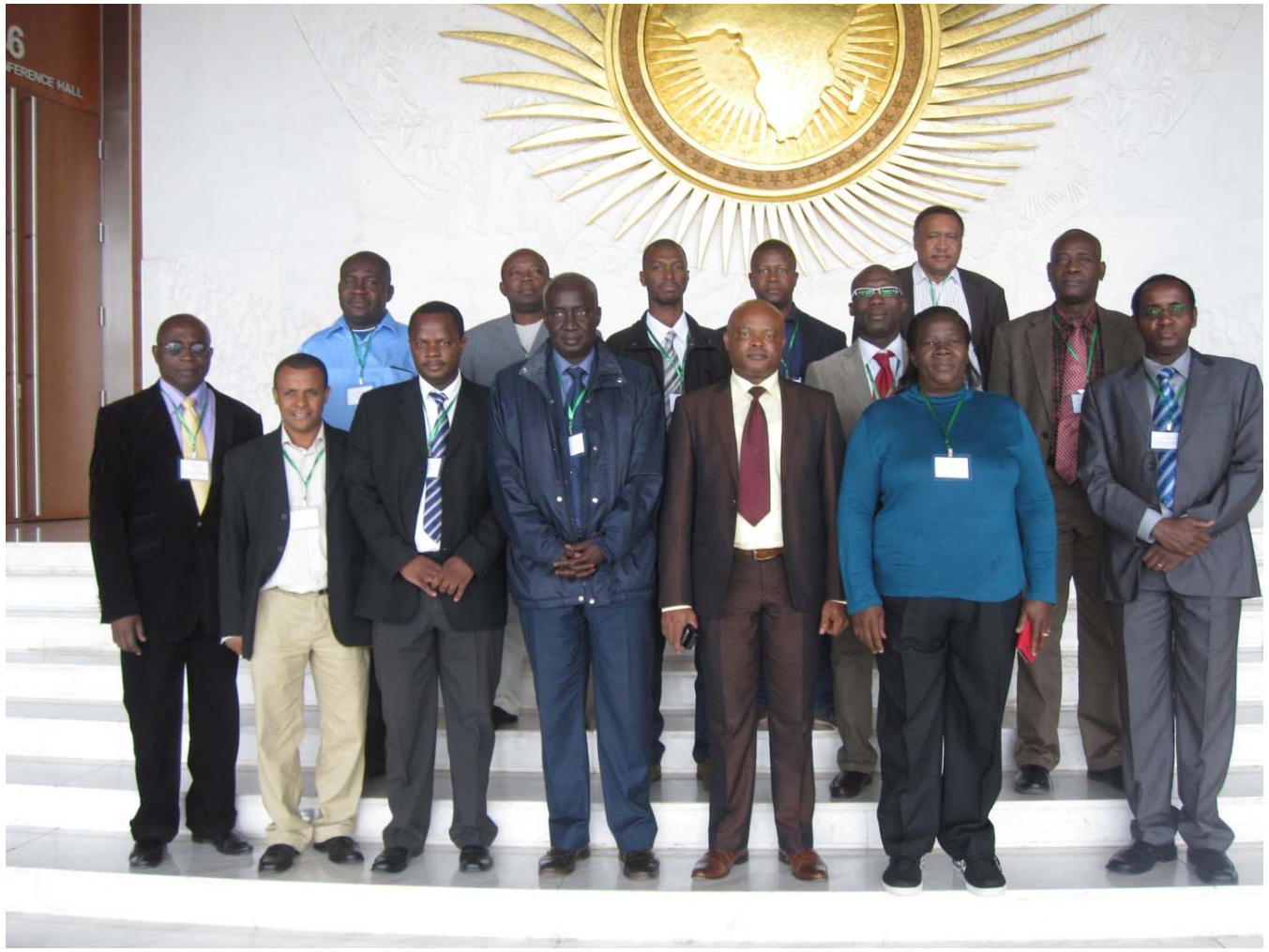
AU-PANVAC activities to support the disease diagnostic

- International Independent Quality Control of Veterinary Vaccines produced in Africa and imported to Africa.
- **Produce and distribute essential biological reagents for animal disease diagnosis and surveillance**
- Facilitate the standardization of veterinary vaccines production and harmonization of their quality control techniques in Africa
- Promote the transfer of appropriate vaccine production technologies in Africa;
- **Provide training and technical support services to veterinary laboratories**.

Identification of Vet. Labs need in diagnostic reagents

- **Consultative Workshop**
  - **Objective of the Consultative workshop**
    - Consult Veterinary Laboratories to:
      - ✓ identify their needs on essential biological reagents for diagnostic of animal diseases.
      - ✓ Develop a strategic framework document for biological reagent production and distribution in Africa.
  - **Participants from 13 AU MS Countries invited**
  - **The workshop took place in AUC Headquarter** (Addis-Ababa, Ethiopia) on 10th and 11th July 2013

Consultative Workshop



Participants at the Consultative Workshop

Issues were discussed during the Workshop:

- Priority animal diseases in each African region (Central, Eastern, Southern and West).
- The challenges faced by member states in the procurement of biological reagents for laboratory activities.
- The importance of the implementation of Quality Management System in all National Laboratories.
- The cost of diagnostic biological reagents.

List of priority animal diseases

- **AU-PANVAC should consider for reagents and assays development**

  - **Rank 1**: Peste des Petits Ruminants (**PPR**), Newcastle Disease (**ND**), Rabies, Lumpy Skin Disease (**LSD**), Africa Swine Fever (**ASF**), Foot-and-mouth disease (**FMD**), **Rift Valley Fever (RVF)**

  - **Rank 2:** Infectious Bursal Disease (**IBD**) or Gumboro disease), **Goat & Sheep Pox**, Brucellosis, Contagious Bovine Pleuropneumonia (**CBPP**), Contagious Caprine Pleuropneumonia (**CCPP**),

  - **Rank3:** Tuberculosis Bovine (**TB**), African Horse Sickness (**AHS**).

Current Reagents and Assays available at AU-PANVAC

- **Monoclonal antibodies generated**
  - **PPR monoclonal antibodies**
    - PPR Mabs were generated and characterized
    - Used in IFA and ELISA.
  - **Mycoplasma (Mccp):** agent of Contagious Caprine PleuroPneumonia (**CCPP**)
    - Mccp Mabs were Generated
- **Well characterised Antisera**
  - PPR (Origin: goat & rabbit)
  - LSD, Sheep & Goat Pox (Origin: rabbit)
  - CCPP (Origin: goat & rabbit)

Current Reagents and Assays available at AU-PANVAC…

- **Assay developed at AU-PANVAC under validation**

  - **PPR: 2 assays**
    - Indirect ELISA (iELISA): Use an antigenic marker specific to PPRV (on N Protein)
    - Blocking ELISA(bELISA): Use a PPRV specific mab (anti-H Protein)
  - **CCPP: 2 assays**
    - Immuno-capture ELISA (ICE)
    - Blocking ELISA(bELISA): Use a specific mab

Conclusion

- **News assays development/improvement on the following field are required: in relation with Trade**
  - Pen-side rapid test for early screening and surveillance of the RVF disease
  - Differentiation Infected from Vaccinated Animals (DIVA) tests
- **AU-PANVAC as per its mandates will contribute to:**
  - Develop new or improve diagnostic assays
  - Produce these assays locally to reduce the cost of diagnostics for labs

THANKS
FOR
YOUR ATTENTION