SABIN VACCINE INSTITUTE

R&D KEY OPINION LEADER CONFERENCE

Monday, April 3, 2023

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Pathways to Licensure: Key Considerations for Filovirus Vaccine Development and Regulatory Harmonization

Keynote Address
03 April 2023

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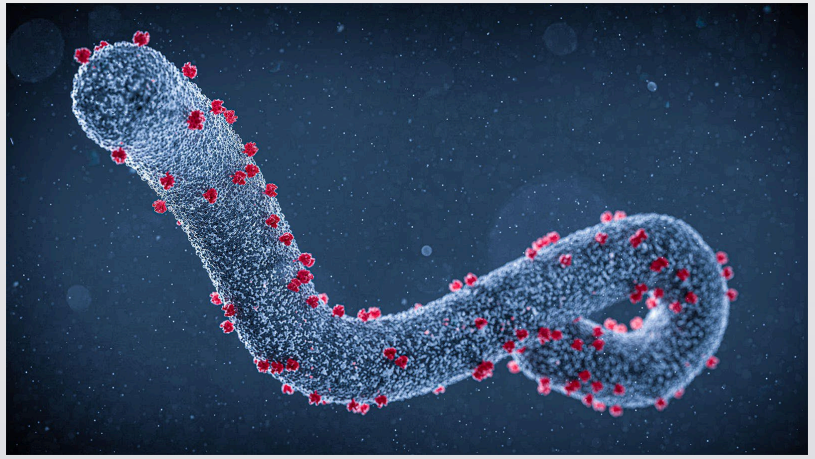
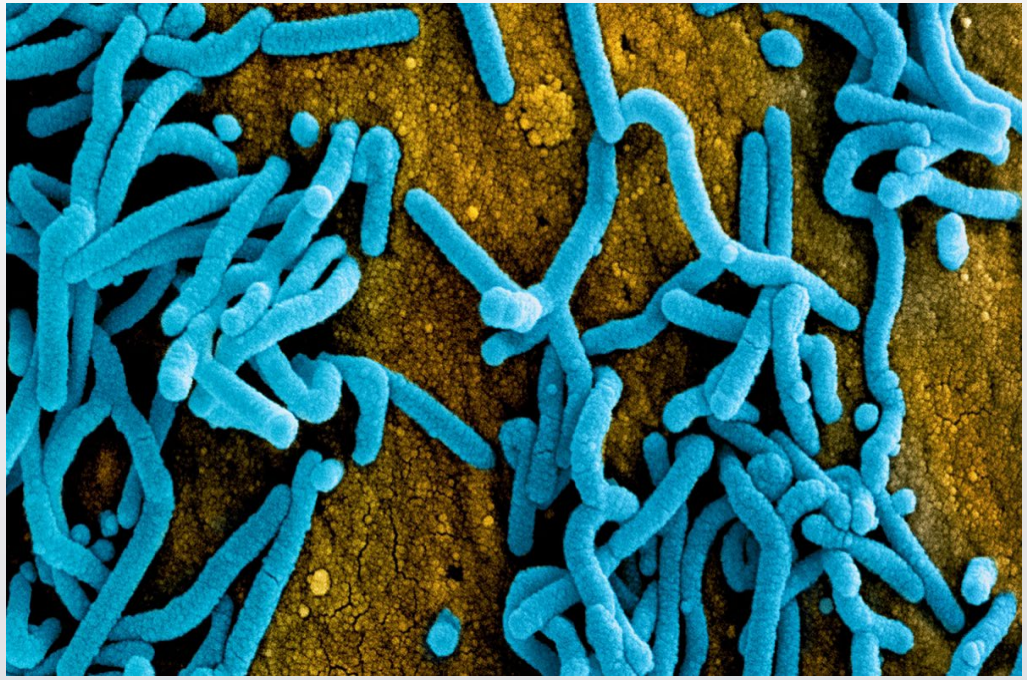


Presentation Outline

- Conflict of Interest
- Introduction to MUWRP
- Epidemiology
- Unmet needs - Why vaccines
- Regulatory Issues
- Ebola Sudan Outbreak in Uganda



Conflict of Interest

- Principal Investigator on a Sabin sponsored phase II Marburg trial to be conducted in Uganda this fall.

- Travel to the conference facilitated by Sabin

Makerere University Walter Reed Project

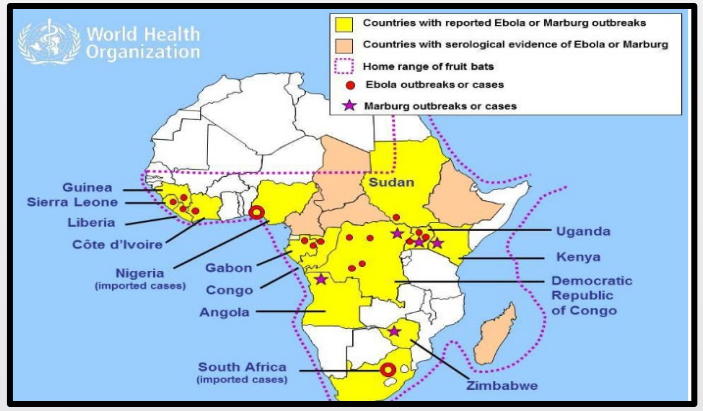
- Autonomous, Uganda registered not-for-profit biomedical research organisation – 20 years of existence:
  - ✓ Vaccine clinical trials (HIV, Ebola, Marburg, COVID-19, Schistosomiasis)
  - ✓ Therapeutics trials
  - ✓ Long term HIV cohorts including individuals at high risk of HIV infection
  - ✓ HIV Cure research.
- CAP accredited laboratory since 2005. able to process biological tissues like lymph node biopsies, rectal biopsies, PBMCs, Biorepository etc
- Surveillance and response to emerging and re-emerging infections
- PEPFAR funded HIV prevention, care and treatment program serving hard to reach areas on the islands of Lake Victoria
- Collaborations with NIH, DAIDS, Henry M Jackson Foundation, Military HIV Research Program, Academic institutions like Makerere, University of Washington, and Pharmaceutical companies like GSK, Sanofi, Janssen

Liquid Nitrogen Plants and Freezers

ILI surveillance in Swine

Epidemiology

- In recent times, Ebola has been in the spotlight- very virulent and fatal illnesses.
  - ✓ West Africa
  - ✓ Outbreaks- DRC
  - ✓ Uganda- Sudan outbreak Sep 2022
- Marburg follows steadily along – Equatorial Guinea and now Tanzania
  - ✓ - Uganda
  - ✓ - Kenya
  - ✓ - Equatorial Guinea
  - ✓ - Tanzania
- Heightened surveillance and preparedness



https://www.cdc.gov/vhf/marburg/outbreaks/chronology.html

Recent and Current Outbreaks

2011

REVIEW 10.1111/j.1469-0691.2011.03535.

Ebola and Marburg haemorrhagic fever viruses: major scientific advances, but a relatively minor public health threat for Africa

E. M. Leroy[1,2], J-P Gonzalez[1] and S. Baize[3]

1) Centre International de Recherches Médicales de Franceville, Franceville, Gabon, 2) MIVEGEC (IRD 224, CNRS 5290, Universités Montpellier 1), Insti de Recherche pour le Développement, Montpellier, France and 3) Unité de Biologie des Infections Virales Emergentes, Institut Pasteur, IFR128-Bioscience Gerland-Lyon Sud, Lyon, France

2014

2022-2023

2023

The largest Ebola outbreak in ever reported reported

Why the Need for Vaccines

MVD

- No licensed vaccines or therapeutics for MVD to-date
- Several trials have been done and planned.

EVD

- Several candidate vaccines tested in human trials
- Monovalent cAD3-EBO Z (Zaire strain alone)
- Bivalent cAD3- EBO (combination of Zaire and Sudan)
- 2 phase I monovalent cAD3- EBO VRC- (Sudan strain alone)

https://theconversation.com/the-uganda-vaccine-trial-how-african-researchers-are-tackling-ebola-121517

Why the Need for Vaccines

- Vaccines remain a critical component for preparedness and response
- Outbreak containment requires, resources and cross-border collaboration to prevent /minimize spread to new regions
- Despite the many outbreaks, countries remain with limited capacity to manage the outbreak. Global multidisciplinary efforts are key.
- With vaccines, transmission and fatality rates may be reduced.

Why the Need for Vaccines

- Progress with Ebola Zaire vaccines and therapeutics
- No vaccine or antiretrovirals against Marburg virus
- This continued reemergence of MARV highlights the need for vaccines to prevent future MVD outbreaks.

Pathways to Licensure of Vaccines

- Three main pathways to licensure
  - ✓ "Traditional" Approval
  - ✓ Accelerated Approval
  - ✓ "Animal Rule"

- All pathways require demonstration of clinical safety and demonstration of effectiveness

So, Which Pathway Then?

Ndomondo-Sigonda *et al. BMC Public Health* (2021) 21:187
https://doi.org/10.1186/s12889-021-10169-1

BMC Public Health

RESEARCH ARTICLE Open Access

Harmonization of medical products regulation: a key factor for improving regulatory capacity in the East African Community

Margareth Ndomondo-Sigonda[1,2*], Jacqueline Miot[3], Shan Naidoo[4], Nelson E. Masota[5,6], Br
Nancy Ngum[2] and Eliangiringa Kaale[6]

Ncube *et al. J of Pharm Policy and Pract* (2021) 14:29
https://doi.org/10.1186/s40545-020-00281-9

Journal of Pharmac
Policy and P

COMMENTARY Open A

Establishment of the African Medicines Agency: progress, challenges and regulatory readiness

Bakani Mark Ncube, Admire Dube and Kim Ward*

- ✓ To promote access to safe, high-quality medicines
- ✓ Mainly generics

Challenges of several regulatory pathways

- Regulatory systems ensure safety, efficacy and quality of medicines and other health technologies.

- LMICs have small markets, limited human and financial resources, making less attractive for product developers hence less developed regulatory systems.

- Pan American Health Organization proposes an approach to regulatory system strengthening that can help them accomplish the most important regulatory functions more efficiently through adoption of efficiencies, such as regionalization and reliance.

Preston C, Freitas Dias M, Peña J, et al. Addressing the challenges of regulatory systems strengthening in small states. BMJ Global Health 2020;5:e001912. doi:10.1136/ bmjgh-2019-001912

Challenges of Several Regulatory Pathways

- Different regions of the world have different regulatory requirements and guidelines for licensure of vaccines and medicinal products
  - ✓makes the licencing processes cumbersome for developers to quickly bring products to the different markets
  - ✓Leads to delays in access of critical medicines and vaccine

- Some of the licensure pathways are less appropriate for filovirus given the need for human efficacy data and the sporadic and short nature of the outbreaks

Is Global Licensure, Harmonization of Possible?

Key Opinion Leader Meeting Series

- "Fostering Global Understanding and Coordination for Ebola Sudan and Marburg Virus Vaccine Development & Licensure Pathways"
- Hosted by the Sabin Vaccine Institute R&D Team (2021 – 2022)

Taken from Slides by Sabin Vaccine Institute

- The European Commission example How did it manage to ***"harmonize inter-state commercial interests while preserving national "autonomy."***

http://dx.doi.org/10.1016/j.jacbts.2016.06.003

- Do we mean harmonization of regulations or is harmonized review ?

This Conference

- To discuss considerations for regulatory approval pathways and harmonization

- Understanding existing regulatory mechanisms to vaccine licensure in the absence of human efficacy data.

- Brings together several stakeholders including regulators, vaccine developers, researchers to gain insights on regulatory alignment

Issues for Consideration

- **Precedence:** Anthrax vaccine licensure – How was it done? Which regulatory pathways were considered during development?
- **WHO pre-qualification** – what is required? What is covered? Ervebo, Zabdeno and Mvabea what do we learn?
- **Lessons from COVID-19 pandemic**, on accelerated vaccine development, emergency use licensure, global collaborations help?
- Are correlates of protection well established? What constitutes an acceptable correlate of protection?

Issues for Consideration

- What clinical or animal data is needed to license a vaccine without human efficacy data? Is this possible?
- **"Nothing for us without us" –** Community preparedness, involvement. How do we ensure public confidence, generating demand, acceptance of vaccines?
- What policies are in place for vaccine roll out? Are they sufficient for filovirus vaccines? How are vulnerable populations catered for? (pregnant women, children, immunocompromised etc)

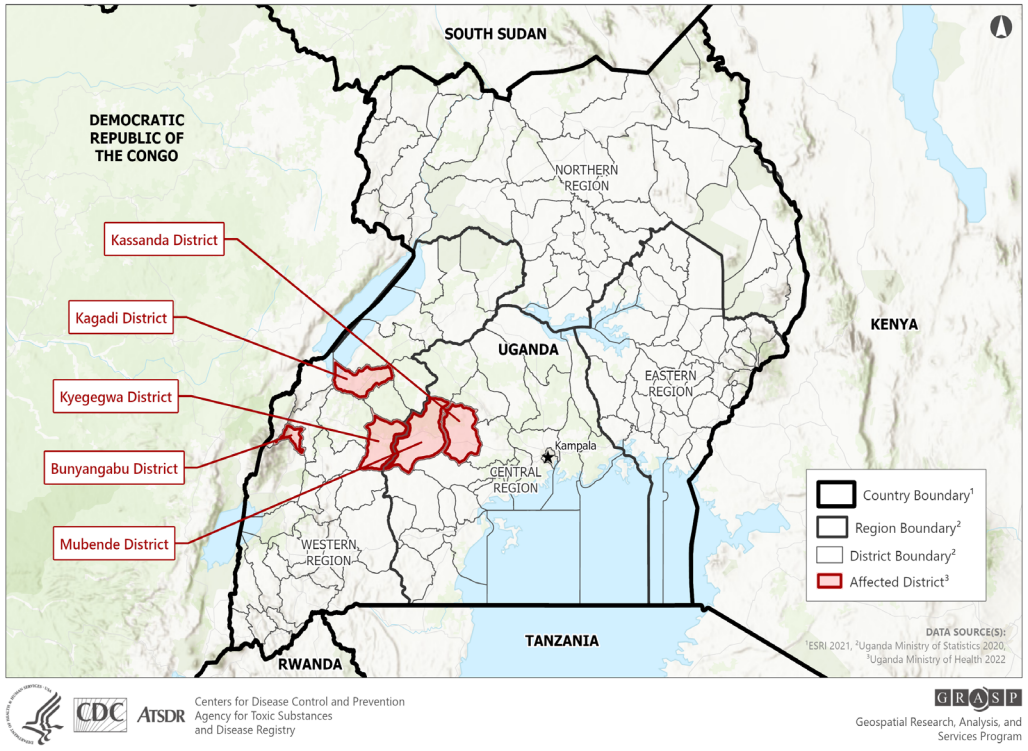
Update on The Recent Sudan Ebola Outbreak in Uganda

Uganda Ebola Outbreak, 2022

- 24-year-old man
- fever, diarrhea, abdominal pain, vomiting blood on 11 September 2022.
- Samples were collected on 17 September 2022 and SVD was laboratory-confirmed on 19 September. The patient died on the same day, five days after hospitalization.
- Declared on 20 September 2022
- Uganda's fifth outbreak with Sudan ebolavirus strain

Ugandan Districts Affected

- Affected the western and central regions of the country



District	Confirmed cases	Probable cases/deaths	Confirmed deaths	Days since the last reported case
Bunyangabu	1	0	0	66
Jinja	1	1	0	23
Kagadi	1	0	1	67
Kampala	18	0	3	20
Kassanda	49	2	21	7
Kyegegwa	4	0	1	37
Masaka	1	0	1	33
Mubende	64	19	28	21
Wakiso	3	0	0	28
Total	**142**	**22**	**55**	

Summary of Cases

- 164 cases (142 confirmed and 22 probable)
- 55 confirmed deaths
- 87 recovered patients
- 19 healthcare workers were infected
- 7/19 of the infected healthcare workers died

National and District Task Force Pillars for Epidemic Response

- Coordination
- Case Management
- Surveillance
- Community Engagement
- Research
- Communication
- Essential Care Services

- WHO
- USAID
- CDC
- UNICEF
- Several other partners including vaccines developers, researchers and donors

Partnerships and Collaborations on Ebola Vaccines

- Vaccines received by MOH (not tested)
  - ✓ 1000 **ChAd3-SUDV** (Sabin Vaccine Institute)
  - ✓ 2,000 **cAdOx1 biEBOV** (Indian Serum Institute's Oxford vaccine)
  - ✓ 2,000 **SV-SUDV** (U.S. manufacturer Merck).

MOH Partners

- WHO
- Coalition for Epidemic Preparedness Innovations(funds vaccine development to prevent pandemics)
- USAID
- CDC
- UNICEF
- Several other partners including vaccines developers, researchers and donors

Vaccines to be tested in the Solidarity against Ebola Trial

Candidate vaccine consignment- Receipt by MoH officials

World Health Organization | Health Topics | Countries | Newsroom | Emergencies

Ebola trial candidate vaccines arrive in Uganda in record 79 days after outbreak declared

9 December 2022 | News release | Kampala, Brazzaville, Geneva | Reading time: 4 min (1175 words)

The first doses of one of the three candidate vaccines against Sudan ebolavirus arrived in Uganda yesterday. These will be evaluated in a clinical trial called the Solidarity Against Ebola or Tokomeza Ebola.

The arrival of the 1200 doses of candidate vaccines just 79 days after the outbreak was declared on 20 September marks a historical milestone in the global capacity to

- The global community was yet again too late!
  - Vaccines not deployed for response
  - Efficacy data not collected

Outbreak was declared over on **10 January 2023**

Ebola National Survivors' Programme

- Established by MoH with support WHO and partners, in the three most affected districts – Entebbe, Kasanda and Mubende to:
  - ✓Maintaining disease surveillance to respond promptly to any flare-up.
  - ✓Stepping up support to 87 people who recovered from the virus
  - ✓Providing comprehensive medical and psychosocial support.

https://www.afro.who.int/photo-story/caring-ugandas-ebola-survivors

Lessons Learned from the Outbreak

- Ability to contain Ebola outbreaks has changed over the several outbreak experiences, new technology, including tests, treatments and vaccines.
- Much improved partner mobilization and coordination leading to faster response
- Mobile P.C.R. test laboratories that can give results in about four to six hours.
- Came off the back of COVID-19 so communities were still aware of need for transmission interruptions
- Experimental monoclonal antibody treatments and remdesivir were used to treat infected health care workers under compassionate use mechanism.
- Important to identify livelihood options, especially for Ebola affected community members.

Outbreak response lab in Mubende

Lessons Learned from the Outbreak

- People are increasingly knowledgeable about outbreaks, and they seek information. Accurate, consistent & constant messaging from the response teams is vital

- Continued capacity building and trainings needed for community surveillance and epidemic response and case management.

- Continued need to handle stigma for health workers, infected persons and volunteers who work on responses – need for psychosocial support cannot be underestimated

- Resource mobilization before and during an outbreak
  - ✓ Emergency funds needed for initial response activities – Most critical!

Lessons Learned from the Outbreak

- "Preventive, not reactive, vaccination is needed to fight Ebola".

A personal take on science and society

World view

By Henry Kyobe Bosa

The case for preventive Ebola vaccination

The Ebola outbreak in Uganda reached major cities. Proactive vaccination is the best way forward.

Uganda's most recent Ebola outbreak should be a wake-up call to the world. Last October, just 3 weeks into the outbreak, the disease spread to Kampala, a well-connected city of 1.5 million people. From there, it might easily have entered other countries.

As the incident manager at the Ugandan Ministry of Health, I coordinated all technical and operational aspects of the Ebola response. We worked tirelessly to curtail the spread, and declared the end of the outbreak on 11 January. But the quarantines and lockdowns came at a high cost

> "The wisest use of this time between outbreaks is to map high-risk areas and vaccinate those in them."

industry was devastating. The societal disruptions that these interventions bring fuel people's anger and distrust of public-health efforts. And they are not the only way to curb the spread of the disease.

Ebola is localized in a band across Central and West Africa. High-risk regions include areas in Uganda, the Democratic Republic of the Congo, Gabon, Sierra Leone, Liberia, South Sudan, the Ivory Coast and Ghana. Certain areas in these countries have evidence of Ebola transmission or are close to the habitats of animals that might be Ebola reservoirs, such as fruit bats. Researchers could map the populations in these countries that are at greatest risk and target them for vaccination, staving off future epidemics.

Mapping would combine three techniques: testing human blood samples for Ebola, testing blood samples from domestic and wild animals and disease modelling

Remaining Challenges

- Advanced vaccines for EBOV. Deliberate efforts to address other strains particularly the Sudan strain and also Marburg
- Understanding clearly the safety, magnitude and durability of responses for the SUDV vaccines
- Further safety evaluations in subpopulations; Pregnancy and immunocompromised populations
- How to incentivize manufacturers to produce the vaccines commercially when demand may not be high enough

Acknowledgements

- All conference organisers, speakers and attendees


Thank
you