Marburg
Candidate Vaccines & Therapeutics
What are the research priorities in the context of an outbreak?

CONCLUSIONS
Conclusions

Dr. Ryan: Importance of global partnership in addressing public health emergencies

Research is essential to assure ultimate availability of safe and effective diagnostics, drugs, and therapeutics for outbreaks, including Marburg. Requires prioritization, funding for vaccines available in vials, trial platforms/protocols, legal/insurance/liability framework, funding for studies.

Index case 7 Jan, Ministry notified 7 Feb. Officially notified to WHO 13 Feb (after positive Diagnosis @ Dakar). Nine deaths- epi links, close family members, burial attendees, 16 quarantine, 15 asx contacts @ home. Response so far: surge field epi capacity, Infx. Prevention & control, case management. 30 day response plan being developed. Past 48 h no new suspicious cases.

MARVAC: WHO-facilitated voluntary working group to foster development of vaccines & therapeutics. Vaccines, animal models, assays.
Conclusions: Vaccines

**Landscape:** Vaccines with protective efficacy in NHPs. Most current efforts involve vectored vaccines. Chad3: Sabin, rVSV: IAVI, PHV, Auro/Emergent, Ad26/MVA: Janssen

**Sabin:** Ph I complete. Small batch produced (2K, 1K used & others committed). Drug substance awaiting filling (20K doses). 850 vialled doses @ VRC part of stability program. Best estimate 100- a few hundred vials available immediately.

**IAVI:** ready for Ph I. Doses available now: 0. Additional process development pending. A few months out

**PHV (Public Health Vaccines):** Angola antigen. Preclinical testing complete. 1 GMP lot has been released (unit dose: 350 vials available- 300 culd be made available). No bulk or active mfg. ongoing. Ph I study pending (but IND is active).

**Janssen:** No active program ongoing but glad to support situation with existing stock, 3500 Ad26 filo (good till April) 2800 Ad26 MARV (need stability testing). All need stability testing before they can be shipped.

**Auro:** Emergent will follow up
Vaccines (conclusions)

Clinical trial core protocol:

Ring vaccination & high risk populations. Individual in hi-risk & transmission clusters or Cluster randomization within transmission clusters (e.g., rings, households, etc.).

Primary endpoint virologically confirmed disease. Also obtain information on efficacy vs. deaths. Primary hypothesis rules out lower bound 30%. Requires 150 cases with Interim analyses @ 50 (67 clusters per arm) & 100 (133 clusters per arm).

In emergency cluster randomization comparing immediate vs delayed vaccination of rings is most feasible.

Implement across outbreaks. Build on lessons learned from Sudan outbreak & tailor to situation in Equatorial Guinea to simplify.
**Therapeutics (conclusions)**

**Mappbio:** in ph I, Remdesivir: doses available for off-label use, Combination may be best based on NHP studies.

**Mappbio:** monoclonal have evaluated 1 & 2 dose regimens in lethal NHP models. FIH healthy volunteer study underway (up to 100 mg/kg). All d 171 f/u complete end 1/23. Limited doses (<30) left over from Ph 1. More material in a few months.

**Remdesivir:** doses available

**3 principles:**
- SOC is essential,
- Integration of research into SOC is essential, conduct trials.
- Support includes buildup of diagnostic capacity, standardized data collection in expanded access.

**Study designs:** placebo controls, factorial design, comparison A vs B vs A+B.
Next steps (with alacrity)

Full sequence information will be available soon. Modeling may help in predicting epidemiology (implications for trials)

Convene Vaccine prioritization committee to consider updated information from developers

Simplify (extract relevant sections from) vaccine clinical protocol for potential use in Equatorial Guinea. Collect safety & immunogenicity data starting ASAP.

Establish standard of care

Identify appropriate context for antiviral use & data collection- including under MEURI, followed by more formal collection of data e.g. using factorial designs.

All decisions will be made by authorities in Equatorial Guinea

MARVAC is an open platform, all with an interest are invited to contribute