

# **Ebola Vaccines and Vaccination**

- **Conclusions and Draft  
Recommendations of the SAGE  
Working Group on Ebola Vaccines and  
Vaccination**



**World Health  
Organization**

# Conclusions

## General

- Based on the available data the Working Group (WG) concluded **that vaccination is likely to provide added value in controlling outbreaks of Ebola Virus Disease (EVD) caused by the *Zaire ebolavirus* (ZEBOV) species.**
- Outbreaks had been curtailed using public health measures other than vaccination. **Vaccination should be part of an integrated strategy** and complement other public health measures in order to effectively interrupt transmission.
- Currently, there **are no data to make any recommendations on vaccines against species of *Ebolavirus* other than ZEBOV** though a bivalent vaccine is under development.
- The **accelerated development of several candidate vaccines is unprecedented** and is a **testament to the value of partnership, participatory approaches and co-ordination.**



# Conclusions

## Safety

- Safety data from Phase 1 studies of **both ChAd3-ZEBOV and rVSV-ΔG-ZEBOV vaccines indicate an acceptable safety profile in healthy adults**. At the time of this recommendation, follow-up of human vaccine recipients did not exceed one year.
- **Arthritis and skin vesicular lesions have been reported in phase 1 studies with rVSV-ΔG-ZEBOV**. While the symptoms subsided in most, 8 reported persistent joint stiffness, whereas 5 reported transient recurrence of joint pain and/or swelling.
- Data on the safety of the rVSV-ΔG-ZEBOV vaccine are **currently insufficient to make definitive recommendations** for vaccination in children. Additional data on the safety of the rVSV-ΔG-ZEBOV in children over 6 years are expected.
- **No data are currently available** regarding the safety of the four leading candidate vaccines in **subjects with underlying disease or medical conditions**. Limited data will become available from ongoing phase 2/3 trials.



# Conclusions

## Immunogenicity

- Both **rVSV-ΔG-ZEBOV** and **ChAd3-ZEBOV** vaccines are **immunogenic** when provided in a **single dose**.
- **Three other vaccine candidates using two-dose schedules have also been evaluated** in clinical trials for Ebola vaccines. These are: (1) recombinant Ad26 and recombinant MVA used in either order; (2) ChAd3 followed by MVA and (3) more traditional two-dose schedule using a recombinant protein based approach. In all 3 cases there is good immunogenicity after the two doses; immunogenicity after two doses (Ad26/MVA, ChAd3/MVA or protein/protein) **appears similar or higher to that seen after one dose of ChAd3-ZEBOV or rVSV-ΔG-ZEBOV alone**.
- From data made available to WHO, the **magnitude of the humoral immune response is similar for ChAd3-ZEBOV and rVSV-ΔG-ZEBOV** vaccines at  $1 \times 10^{11}$  and  $2 \times 10^7$  dose levels, respectively, 28 days following vaccination.



# Conclusions

## Efficacy/ effectiveness, registration and programmatic feasibility

- There are efficacy and effectiveness data from an interim analysis of a phase 3 trial of the rVSV-ΔG-ZEBOV vaccine in Guinea. **The results of this interim analysis suggest that rVSV-ΔG-ZEBOV is efficacious (efficacy= 100%, 95% CL 74.7-100, p=0.0036), safe, and likely to be effective at the population level (effectiveness=75.1%, 95% CL -15.5 to 95, p=0.1791) when delivered during an EVD outbreak using a ring vaccination strategy.**
- The WG takes note of the fact that the rVSV-ΔG-ZEBOV vaccine **ring vaccination trial has been expanded from the Guinée Maritime to Sierra Leone.**
- Although data on the available candidate vaccines, including efficacy data for the rVSV-ΔG-ZEBOV, is accruing, **current regulatory approvals are limited to the use of vaccine in a clinical trial setting.**
- In a trial setting, it was **possible to deliver vaccine at the community level while maintaining the stringent cold chain requirements (i.e. - 80° C). Studies are ongoing to evaluate the thermostability** of different vaccines at temperatures more suitable for delivery of vaccine at the community level.

# Draft recommendations

## Preamble

- Based on the review of current data on disease epidemiology, risk factors for infection and death from EVD, disease transmission patterns and projected impact of vaccination using different delivery strategies under different epidemiological scenarios, the WG proposes the following **provisional** recommendations for consideration by SAGE. **These recommendations may need to be reviewed and revised in light of the emerging data on the different vaccines.**
- The currently **available evidence only allow for recommendations for reactive vaccination** (i.e. in response to an outbreak). The evidence is insufficient to formulate recommendations for preventive vaccination (i.e. in the absence of any cases).



# Draft recommendations

## Preamble

- While the rVSV-ΔG-ZEBOV vaccine and other candidate vaccines are currently being used in the context of a clinical trial, **recommendations for use outside a trial setting will depend on the vaccines receiving regulatory approval** (i.e. full licensure, conditional licensure or emergency use authorization outside a clinical trial setting).
- These **draft recommendations are prepared on the basis of interim trial results suggesting high efficacy of the rVSV-ΔG-ZEBOV vaccine and immunogenicity data for the ChAd3-ZEBOV that suggest that it is comparable to rVSV-ΔG-ZEBOV**. However, it is important to note that the **recommendations do not apply to any specific vaccine. Vaccine-specific recommendations will be made once a vaccine is registered for use outside a trial setting**. Meanwhile, it is **important that the development and evaluation of other candidate Ebola vaccines continue**, as there may be a need for alternative vaccines with different characteristics more suited for certain conditions or in specific target populations.





# Draft recommendations, provisional to regulatory authorization

- **Objectives of vaccination:** The main objectives for vaccination are interruption of transmission and individual protection for those at high risk for infection
- **Target populations:** all eligible individuals should be vaccinated as per the chosen vaccination strategy, certain high-risk groups merit special consideration
  - Health care workers (doctors, nurses, laboratory workers)
  - Other categories of health workers (mid-wives, surveillance staff, radiographers, cleaners and laundry workers)
  - Other groups at high risk of exposure
    - Informal health service providers (traditional healers, herbalists etc.)
    - Those involved in funeral rites (elders, religious leaders, senior members of secret societies, and traditional washers)
  - The categories of front-line workers and other risk groups may vary from one community to the other and may need to be defined locally



# Draft recommendations, provisional to regulatory authorization

## ● *Vaccination delivery strategy:*

- Delivery strategy of choice will depend on the extent of the spread of disease, the number of cases being confirmed per week at the time when vaccination is initiated, the status of implementation of other public health measures, the effectiveness of contact tracing and the available supply of vaccine.
- Potential strategies include ring vaccination, geographic targeting of an area (mass vaccination) and front line worker vaccination.
- When more data are available, it may be possible to provide more precise recommendations on the choice of vaccination strategy.

# Considerations for improving acceptability

- Pregnant women and infants have very high CFR. They may be protected by indirect protection if others in the community are vaccinated. **Inclusion of pregnant women as a means to indirectly protect their infants and young children might need consideration in the future.**
- **A communication strategy tailored for the affected communities** should be considered, including:
  - Public vaccination of community leaders (e.g. religious leaders, members of Parliament, chiefs, etc.).
  - Information provided on an anticipatory, iterative and responsive basis to address rumors, anxieties and resistance. Appropriate media including m-Health messaging, should be utilized in the affected communities if pertinent.
  - Engaging survivor networks for advocacy to enhance the acceptability of vaccination.
- The work of the **Global Ebola Vaccine Implementation Team (GEVIT) to develop tools and generic deployment plans** is critical to ensure the timely and successful deployment of any vaccine(s) and should be completed **as soon as possible**.

# Recommendations for further research

- The WG requests **researchers to share data from pregnant women and immunocompromised subjects vaccinated during the ongoing trials** once they become available. **All future trials should consider collecting data on the safety and immunogenicity of the respective vaccine candidates in children and adolescents, pregnant and lactating women, and immunocompromised individuals.**
- WG recommends **continued efforts to develop and evaluate vaccines against filoviruses other than ZEBOV**, such as Sudan, Bundibugyo and Marburg. Multi-valent filo virus vaccines are desirable. The WG is encouraged by efforts to develop a bivalent *Zaire-Sudan ebolavirus* vaccine.

# Recommendations for further research

- **All trials should carefully document adverse events using standard definitions**, including duration, severity and sequelae. In particular, for rVSV- $\Delta$ G-ZEBOV vaccine, safety monitoring should document and clearly distinguish arthritis from arthralgia.
- Future studies should **evaluate the feasibility and effectiveness of the delivery approaches**, duration of protection, and measures that ensure high levels of community acceptance.
- **Future research should implement community-based participatory approaches** to engage participants in all stages of clinical trials, including design, monitoring and evaluations.

# Recommendations for further research

- **Pre-approved and pre-positioned protocols and local research capacity strengthening** in countries at risk for future outbreaks should be put in place now to facilitate rapid implementation of relevant studies including assessment of newer vaccine products, in the event of future outbreaks. Such protocols are included in the blueprint for conducting research during public health emergencies, which is currently being developed under the leadership of WHO.
- **The ongoing efforts to model the impact of different Ebola vaccination strategies** on preventing disease and transmission should be pursued and expanded to further inform the understanding of their respective value in controlling an outbreak.