CONCEPT NOTE

Consultation on expedited implementation of the listing recommendation of Ebola vaccine in Africa

Reference: PQT-CR-2018-119

Background

Ebola Virus Disease (EVD) is caused by one of five species of Ebola viruses, namely, Zaire, Sudan, Tai Forest, Bundibugyo and Reston, with the most fatal specie being the Zaire virus (REF). Over the years, there have been several outbreaks in Democratic Republic of Congo, Uganda, Sudan, Gabon and Congo. The last major outbreak occurred in 2014-2015 in countries of West Africa subregion, mainly in Liberia, Guinea and Sierra Leone and to a lesser extent Nigeria and Mali. This was the largest EVD outbreak to date, and a total of 28,616 Ebola cases were reported in the three most affected countries (Guinea, Liberia and Sierra Leone), with 11,310 deaths. A significant proportion of survivors have both short- and long term sequelae.

At the time of the outbreak, there was no effective vaccine against the virus and all the vaccine candidates were in very early phases of clinical development.

In consideration of the urgent need for vaccines against EVD being available, WHO developed the Emergency Use Assessment and Listing (EUAL) as a process to expedite the availability of vaccines needed in public health emergency situations. The EUAL is a special procedure intended to assist interested UN procurement agencies and Members States (MS) in the acceptability for use of specific vaccines in the context of a public health emergency, based on an assessment of minimum set of available data.

The EUAL process generates WHO recommendations that provide advice to procurement agencies and MS on the acceptability of a specific vaccine in the context of a public health emergency. These recommendations are based on: 1) a minimum set of available quality, safety, and efficacy data; 2) a plan for further evaluation of safety and effectiveness; and 3) a plan for subsequent prequalification of the product.

In order to facilitate potential submissions as well as the assessment process under the EUAL procedure, the WHO prequalification team (PQT) had exceptionally decided to accept "rolling on submissions": i.e. manufacturers can submit data sets as soon as they become available.

Merck & Co., Inc. submitted data on their rVSVΔG-ZEBOV-GP (V920) vaccine (a Live Attenuated Ebola Vaccine). This vaccine underwent clinical trials (CT) phase I and II in 2014-2015 in Europe North America and Africa and was consequently used in Guinea in 2015 during ring vaccination campaigns while going through CT phase III.

The evaluation was based on a benefit-risk assessment of available quality, safety and efficiacy data and the severity of the disease since some of the essential information is not yet available. The vaccine experts considered that this vaccine could be used at the next outbreak. The view of the experts is that the currently available safety, immunogenicity and efficacy data would support an Emergency Use Assessment and Listing for V920 vaccine provided that the genetic structure of the virus in a new outbreak would not differ too much from the virus that circulated in Guinea when the vaccine was used during CT in 2015.

The Strategic Advisory Group of Experts (SAGE) recommended :

that the use of the rVSVΔG-ZEBOV-GP candidate vaccine should be deployed under the Expanded Access framework. The recommended delivery strategy is ring vaccination adapted to the social and geographic conditions of the outbreak and affected areas. Pre-emptive vaccination of health care workers is not recommended as current evidence is insufficient to support this. In addition, at present, available evidence is insufficient to recommend pre-emptive mass immunization of the general population because of the still partial knowledge on the vaccine immunogenicity, efficacy and safety.

During a teleconference with members of the AVAREF Steering Committee and the Technical Coordination Committee , it was agreed that Secretariat should convene a meeting to:

- raise awareness of the EUAL
- discuss the Merck vaccine and the EUAL recommendation
- address practical issues on how EUAL could be translated into the appropriate regulatory decisions in the targeted countries.

In preparation for this meeting, it was agreed that:

- WHO would share with the steering committee the EUAL benefit/risk assessment report performed by WHO prequalification team.
- The secretariat to involve relevant countries in the meeting, with at least one representative with relevant experience from each potential or currently affected country, with relevant experience, to look at the actual issues for country approval and post-approval data collection.
- The Technical Coordination Committee of AVAREF will be engaged.

Objectives of the meeting

1) To present the EUAL procedure

2) To describe the review process and conclusions from experts based on available information and risk-benefit analysis

3) To discuss issues and possible mechanisms related to the use of the WHO EUAL recommendation in potentially affected countries.

4) To brainstorm on ways to optimize synergies between AVAREF and WHO to assist countries in efficiently implementing the listing recommendation in affected and potentially affected countries and to prepare a plan of action

5) To provide a preview of the new EUL, discuss optimal involvement of local authorities and prepare a proposed plan of action for endorsement by AVAREF

6). To discuss issues that could hamper the use of the listed vaccine in the countries, how to mitigate them, and how to address safety and effectiveness data collection.

Expected outcomes

- A strategy for expediting the authorization and deployment of the vaccine at the country level

- A proposed plan of action to support the post deployment handling of the vaccine and monitoring of safety and effectiveness

- A proposed strategy for AVAREF to optimize its level of involvement during the three phases of the new EUL procedure

Participants

- Members of the Steering Committee and Technical Coordination Committee of AVAREF

- Staff from regulatory authorities and Ethics Committees with expertise in regulatory evaluation of vaccines, safety monitoring, approval of clinical trials and market authorization.

Tentative program

Day 1

Session 1: Background, objectives and expected outcomes

9:00-9:15	Opening: Nomination of chair and rapporteur and roles
9:15-9:30	Introductions
09:30-09:45	Objectives, format of the meeting and expected outcomes

Session 2: WHO policy recommendations

09:45-10:15 Update on the current status of Ebola outbreaks (WHE)

10:15-10:45	Coffee break

Session 3 Overview of the EUAL procedure and assessment of Ebola vaccines and role of AVAREF facilitating access of priority public health.

10:45-11:10	Overview of the procedure
11:10-12:00	Information submitted for Ebola vaccines- Conclusions of the review
12:00-13:00	Discussion
13:00-14:00	LUNCH
14:00-14:30	Overview of AVAREF

Session 4: Considerations and required actions in the efficient implementation of the listing recommendation

14:30-14:45	Introduction
14:45-16:00	Discussion

- Legal provisions to authorize use of products in an emergency
- Options to facilitate reliance on WHO EUAL

16:00-16:30 Coffee break

16:30-17:15 Continued discussion

- Strategy and action plan for reliance on EUAL in case of a possible expansion of the outbreak

- Activities that countries can launch to ensure proper use of vaccine (cold chain, open vial policy, etc)
- Collection of safety and effectiveness data
- Role of AVAREF in facilitating authorization for use, proper use and data collection/surveillance

17:15-17:30 Wrap up: List of recommendations and Action points

Day 2

Session 4: Considerations and required actions in the efficient implementation of the listing recommendation (continued)

9:00-10:45 Continued discussion

10:45-11: 15 Coffee break

Session 5: Preview of the new EUL and discussion on optimal involvement of potentially affected countries

11:15-11:35 Overview of the new EUL

11:35-12:00 Discussion

12:00-13:00 Lunch

13:00-14:00 List of recommendations and action points

Closure