Q&A on trial of Ebola Virus Disease vaccine in Guinea

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A. CLINICAL STUDY AND VACCINE

1. What is a vaccine clinical trial?

Development of new vaccines starts in laboratories. When researchers have sufficient evidence that a vaccine appears safe and effective, they must ensure this is also the case in humans through reliable scientific studies called “clinical trials”. This step is crucial before vaccinating a large number of people.

There are several types of studies (called "phases") that progressively test safety. A Phase I study is done to ensure the vaccine does not injure the person being vaccinated, beyond possible fever or other minor inconveniences. Phase II studies look at the human body's ability to mount a defence. This is also known as an immune response, or the way in which microorganisms are destroyed in the vaccinated person’s body. In Phase III, the effectiveness of the vaccine – that is, does it prevent disease – is the focus.

2. Which vaccine is being used in the trials in Guinea?

The vaccine used in the Guinea study is called rVSV-ZEBOV. Despite its complicated name, it is basically a "good" microorganism that has borrowed the guise of the Ebola virus, but it does not contain Ebola virus. It cannot cause Ebola virus disease, but this "good" microorganism manages to trick the body of the vaccinated person and triggers an immune defence against Ebola virus. If the vaccine is effective and if a person who has been vaccinated comes into contact with the real Ebola virus, their defences are ready and they will be able to eliminate the virus without getting sick.

The vaccine was developed by the Public Health Agency of Canada and NewLink Genetics USA and is manufactured by Merck Vaccines USA in the United States of America.

3. Is the vaccine in use elsewhere?

More than 800 people in Canada, Germany, Gabon, Kenya, Liberia, Switzerland, and the United States of America, have been vaccinated with rVSV-ZEBOV since October 2014. A clinical trial was started on 7 March in Guinea. Since then, more than 200 additional volunteers have been vaccinated. To date, no serious adverse effects have been reported.

4. Can the vaccine cause unpleasant or dangerous reactions in people who have been vaccinated?

After vaccination, some volunteers have experienced “flu-like” symptoms, (that is, symptoms similar to what many experience when they get influenza). In the first 24 hours after vaccination, they might
develop some fever, chills or headaches, or feel fatigue or muscle pain. These reactions usually last no longer than a few hours and disappear with medication to bring the fever down. Some volunteers also experienced joint pain, beginning in the first two weeks after vaccination and generally lasting no more than a few days.

5. Is now the right time to carry out this clinical trial in Guinea?
Efforts to eliminate Ebola virus disease in Guinea have fortunately resulted in the elimination of cases in most of the country, except in Lower Guinea (Basse Guinée). This is why it is urgent to step up the clinical study. If the vaccine is effective, it can be used to eliminate the virus in all prefectures where it is still present. It may also be used in other countries to prevent the spread of future Ebola virus disease epidemics.

6. Who authorized this clinical study in Guinea?
The study is being supervised by the Government of Guinea. The study protocol was reviewed and approved by the National Directorate of Pharmacies and Laboratories and the National Ethics Committee for Health Research. Independent committees responsible for the ethical review of projects implemented in partnership by the World Health Organization (WHO), Médecins Sans Frontières (MSF), and the Norwegian National Institute of Public Health also studied the protocol and approved the clinical trial.

7. What are the objectives of the Ebola vaccine clinical studies in Guinea?
In Guinea, two clinical trials are being carried out: a Phase II clinical study to vaccinate frontline workers, for whom the occupational risk of contracting Ebola disease is the highest, and a Phase III clinical study, using a trial design called “ring vaccination”. In addition to providing reassurance that the vaccine is safe for humans, the trial also aims to demonstrate that the vaccine can effectively prevent Ebola virus disease. This evidence will facilitate introduction of the vaccine on a large scale, supplementing other measures to prevent Ebola virus disease.

An international group of experts from Guinea, along with experts from Canada, France, Norway, Switzerland, the United Kingdom, the United States, and the World Health Organization (WHO) has developed the clinical trial.

8. What is the scientific basis for ring vaccination?
The ring vaccination strategy is based on the approach used in the 1970s to eradicate smallpox. The implementation of this strategy involves the identification of a newly diagnosed and laboratory-confirmed case of Ebola virus disease — “patient zero” — and the tracing of people who have been in contact with that patient. These people and their contacts — often family members, neighbours, colleagues, and friends of the patient — will constitute the “ring”, generally made up of 50 to 100
individuals. The individuals in the ring are vaccinated, if they give their consent. The rings are selected at random for immediate or delayed vaccination (after 21 days).

Ring vaccination has two objectives: (i) to test whether the vaccine protects people who have been in contact with an Ebola patient and (ii) to ensure that the vaccination of persons who are in the “ring” manage to create a buffer zone — or protective ring — around “patient zero” to prevent the spread of infection.

To assess the efficacy of the vaccine, some rings will be vaccinated as soon as “patient zero” is identified (immediate ring vaccination) while other rings will be vaccinated three weeks later (delayed ring vaccination). This strategy will allow researchers to draw a comparison between the different rings and avoid using a placebo (or inactive control) that would otherwise be administered to half of those taking part in the clinical trial.

9. Who will be vaccinated?

A clinical study is not a vaccination campaign and there are strict pre-established criteria for defining who may or may not be vaccinated.

In this study, “frontline workers” have been identified as a target population due to their professional activities, which bring them into contact with people infected with Ebola or with the virus itself. This can include doctors, nurses, paramedics, laboratory staff, cleaning staff, and burial teams.

The “ring vaccination” part of the clinical trial targets people who have had contact with confirmed cases and contacts of these contacts.

Like any clinical trial, participation is voluntary and only eligible persons who give their consent will be vaccinated. Persons under 18 and pregnant women will not be vaccinated.

10. When and where did vaccination start?

The ring vaccination part of the clinical trial is being rolled out in areas of the country where a number of cases of Ebola virus disease have been reported. Currently, this means prefectures in Lower Guinea. If the epidemiology changes in the coming weeks, the site of the trial could be changed.

The clinical study focusing on the vaccination of frontline health workers began on 7 March 2015 with the vaccination of Guinean officials. Frontline workers have been vaccinated since 25 March, starting with health workers from Donka hospital in Conakry.

A second ring vaccination clinical study began on 23 March in Coyah Prefecture. Since that date, additional rings in Coyah and Conakry have been vaccinated. Before vaccinating, every effort was made to ensure that preparations complied with international standards; for example, in the area of good clinical practice. Staff training, improved procedures to collect and analyse data, logistics and resources, and community involvement in the trial area are other essential components of preparation.
B. CLINICAL TRIAL PARTNERS

11. What partners are supporting or financing this initiative?

The World Health Organization (WHO) is sponsoring the clinical trial.

The implementation of the trial involves a number of international partners, coordinated by the Government of Guinea. These partners include WHO, Médecins sans Frontières (MSF), Epicentre, the Norwegian Institute of Public Health (NIPH), and the European Union Mobile Laboratory in Guinea (EMLab).

Funding is provided by MSF, the Norwegian Research Council through NIPH, the Government of Canada through Public Health Canada, the Canadian Institutes of Health Research, the International Development Research Centre and the Ministry of Foreign Affairs, Trade and Development Canada, and WHO with support from the Wellcome Trust (United Kingdom).

12. What are the roles of the various field partners in Guinea?

MSF and Epicentre are focusing on the vaccination of frontline workers, specifically health workers in the Ebola treatment centres.

WHO is focusing on the logistics and implementation of ring vaccinations, because this part of the trial relies on contact tracing carried out by surveillance staff who are also involved in the Ebola response effort and in many cases are staff members of the Organization. WHO is also responsible for the management of the data collected and for adherence to good clinical practices.

EMLab in Guinea is responsible for processing blood specimens taken from the frontline workers to determine if the vaccine is “immunogenic”, i.e. if it triggers a reaction against the Ebola virus in the body of the vaccinated person. EMLab is also involved in confirming the diagnosis of Ebola disease in those designated as “patients zero” or any person in the clinical trial who presents with signs or symptoms consistent with Ebola virus disease.

13. What will happen once the Guinea ring vaccination clinical trial is completed?

The clinical study focusing on the vaccination of frontline workers and the ring vaccination clinical study are being conducted simultaneously. It is estimated that the two protocols could complete their respective vaccination of volunteers over a three-month period. This will be followed by an observation period of 84 days after vaccination. If the ring vaccination trial demonstrates the efficacy of the vaccine, wider use of the vaccine could be considered after August 2015.

Financial resources are in place to procure and supply the vaccine to the countries affected by Ebola virus disease. Millions of doses will be financed, if necessary, by the Global Alliance for Vaccines and Immunizations (GAVI), whose Executive Board approved a budget of US$ 300 million in December 2014. An additional US$ 90 million has been earmarked to support the roll-out of the vaccine.