Third teleconference on vaccine clinical trials design for Guinea, Liberia, and Sierra Leone

18 December 2014

Presenters: Drs A. Henao Restrepo (WHO, for the Guinea Collaboration); S. Kargbo (Sierra Leone); S. Kennedy (US NIH, for Liberia); R. Phillips (Newlink-Merck); A. Schuchat (US CDC); R. Ballou (GSK); J. Van Hoof (Johnson & Johnson)

Agenda
The specific purpose of this teleconference was to update participants on:
- preparations for Phase III clinical trial in Liberia
- preparations for Phase III clinical trial in Sierra Leone
- preparations for Phase III clinical trial in Guinea
- new results on ChAd-ZEBOV candidate vaccine
- new results on rVSV-ZEBOV candidate vaccine
- next steps on clinical development of Ebola vaccines

Liberia: Dr S. Kennedy, US NIH
The Phase III clinical trial protocol was reviewed during a two-day workshop in Monrovia, with technical teams from the Liberia and the United States (US). One of the major achievements was to set up a group to finalize the protocol and prepare for field operations. Over the past few weeks, the group has targeted key opinion and community leaders to begin community engagement. The group is preparing a social mobilization plan for January 2015.

The protocol has already been submitted to the US FDA and submission to the Liberian authorities is expected by the end of 2014.

Site preparation will start at the end of 2014. The current planned start date is between 12-19 January 2015.

Sierra Leone: Dr S. Kargbo, Sierra Leone and Dr A. Schuchat, US CDC
Strong working relationships have been established between the Ministry of Health in Sierra Leone, including at District level, and MSF, CDC, and WHO.

In order to prepare for regulatory and ethical submissions, Sierra Leone is working closely with countries that have strong, established ethics committees.

It was reported that many health-care capacities are closed and, as a consequence, health-care staff have relocated elsewhere. This makes it challenging to determine the size of population eligible for the study. This requires additional effort, especially for the CDC staff based in the districts.
Sierra Leone is ready for post-vaccination surveillance. The Connaught Hospital in Freetown is the main hospital, and it will be used for monitoring of adverse effects.

A protocol has been developed for community engagement and social mobilization in collaboration with NGOs.

Assessment of cold chain needs and capacity is ongoing.

Phase I data are still being reviewed and therefore the final choice for the vaccine for the Phase 3 efficacy trial has not yet been made. An option for a prime-boost protocol is still open.

The trial may start during the second half of January.

**Guinea/Dr A.M. Henao Restrepo on the behalf of the Guinea Collaboration**

The Phase III protocol was sent to the Guinea Collaboration’s working group and received constructive comments regarding trial design and potential partnerships. The final version is now available. Standard operating procedures in French should be available by the first week of January,

Discussions are ongoing with partners in the Collaboration to determine the role of each entity. Among others, John-Arne Rottingen from Norway will chair the Study Steering Group, the Guinean Ministry of Health and MSF will be in charge of field operations, and WHO will take responsibility for data management and analysis.

The protocol was submitted to the national regulatory agency and ethical committee in Guinea for comments and/or approval.

For the ring vaccination study, the focus will be on the determination of protection against Ebola virus disease in order to assess effectiveness of vaccination, and immune responses will not be analyzed. For the frontline workers’ study, the Guinea Collaboration will focus on determination of potential serious adverse events. Blood samples will be frozen for later analyses.

The vaccine to be used in the efficacy trial has not yet been determined. For the moment only one dose is being considered, but the discussion is still open. The trial should be able to start in January-February 2015.

**GSK/ Dr R. Ballou**

Immunization of all volunteers in the various Phase I trials with ChAd-ZEBOV is completed. Immunogenicity data are expected around 12 January 2015. For the moment, the safety profile is very good and any dose-level could thus be selected.

Manufacturing is on track and enough vaccine will be available for the efficacy trials.
J&J, Dr J. Van Hoof
In early January, the J&J company will start Phase I clinical trials, which are planned in Africa, the UK, and the US.

All options are open for efficacy trials.

NewLink-Merck, Dr R. Phillips
The company has produced 30,000 doses rVSV-ZEBOV at $1 \times 10^8$ and 30,000 doses at $3 \times 10^6$ pfu/mL. Enough vaccine will be available to run efficacy trials. Arthritis with grade one pain in small joints (mainly in the fingers) has been recorded in the Geneva trial (c.a. in 20% of volunteers at $1 \times 10^7$ and $5 \times 10^7$). This is not considered as a matter of concern.

Next Steps
A second high-level meeting on Ebola vaccine access and financing will be organized by WHO in Geneva on 8 January 2015. The purpose of the meeting is to bring progress to the attention of policy-makers and other stakeholders.