First teleconference on vaccine clinical trial designs in Guinea, Liberia, and Sierra Leone
28 October 2014

The meeting was chaired by WHO Director-General, Dr Margaret Chan, and co-chaired by the Deputy Director-General, Dr Anarfi Asmoa-Baah.

Dr Chan welcomed the 48 participants on the call and thanked them for their time and expertise. She explained how the call responded to specific requests made during the 23 October High-level Meeting on Ebola Vaccines Access and Financing, and reflected the meeting’s sense of urgency.

The purpose of the teleconference was to critically assess proposed protocols for phase 2 and 3 clinical trials.

Participants in the teleconference looked at four proposals.

1. From the NIH for Liberia, a protocol for a randomized, controlled phase 3 safety and efficacy study that compares the GSK and the NewLink investigational vaccines.
2. From the CDC for Sierra Leone, a stepped-wedge study design that phases in vaccines for high-risk populations while informing broader use.
3. From Kader Konde, three proposed phase 2 and 3 trials to be conducted in Guinea: a study in frontline workers, a ring vaccination trial, and a booster trial.
4. An offer from Johnson & Johnson of support with their two vaccines as a possible third arm to the randomized, controlled NIH trial in Liberia.

Liberia
For the study in Liberia, NIH staff and a protocol team are right now in Liberia refining the protocol. Given the importance to getting early but valid answers to questions about community engagement, acceptance of vaccines, sensitivities about randomization, and logistical challenges, the protocol team was working with officials from the Ministry of Health, UNICEF, USAID, WHO and others. A Community Advisory Group had been formed. A more detailed protocol will be ready when these and other technical issues have been explored and resolved.

During the discussion, questions were raised about inclusion and exclusion criteria, acceptability of the study to participants, which control vaccine will be used, whether the control group will receive vaccine, what to do if waning efficacy is detected, and how long follow-up will continue. Concerning whether a subset of immune correlates will be used, NIH replied that it was doubtful whether these correlates would be known.

For its part, industry had submitted written comments on the protocol. All were eager to see the next iteration as the study design continues to evolve.

Sierra Leone
Likewise, for the CDC study in Sierra Leone, a team is right now on the ground, also to help solve logistical challenges. The study, which will use a cluster randomized enrolment design, will be looking at adult health care workers in Ebola treatment centres, other health care workers at enhanced risk, and other frontline workers. Initial signs are that the studies will
be acceptable to these workers. In the field, the study is expected to improve surveillance and case detection among health care workers.

Both industry and regulatory authorities expressed their keen interest in the study. The protocol will benefit from pre-clinical toxicology studies and dose-selection data.

Questions were raised about the feasibility of an investigation that trials 2 vaccines. Are there enough discrete units in Sierra Leone to trial 2 vaccines. Will the trial stop too soon? These and other questions were answered as CDC clarified the study design and certain misperceptions that arose from the requested brevity of the report.

Guinea
The three proposed studies, which are in the early stages of development, provoked considerable discussion. All agreed that Guinea must not be left out. Several refinements to the protocols were proposed. Industry was concerned that the study of frontline workers has no control group, introducing significant opportunities for bias. Start dates and study populations were likely too ambitious. Particular interest focused on the ring vaccination study and the investigation of booster doses. Several offers of support to refine the study protocols were made, also from France and Norway.

J&J
The company was coming slightly later with candidate vaccines but nonetheless expressed its strong desire to be involved. The advantages of its two-dose prime-and-boost approach were briefly discussed.

In general
MSF drew attention to constraints in the field, the need to engage communities, the logistical challenge of storing vaccines at minus 80°C in hot tropical climates, and the need to deal with high expectations and possibly misplaced hope that the promise of vaccines is almost certain to provoke.

Canada expressed interest in supporting the stepped-wedge study in Sierra Leone, in close collaboration with CDC and the governments of the UK and Sierra Leone. On the randomization issues, consultation might be needed with experts on the ethical dimensions of clinical trials.

The UK offered to quickly set up a small yet visible working group of scientists who could give a “third-party” assessment of the scientific dimensions of prime-boost study protocols. This proposal was considered useful by many, also as a resource that could expedite the work of regulatory authorities. For example, such a small group of scientists could help clarify some of the prime-boost issues. Others hesitated over the very short timelines proposed, especially as intense work on finalizing the protocols in Liberia and Sierra Leone was under way. Nothing should come up that might delay that work.

The group decided:
- That the protocols for Liberia and Sierra Leone should be further pursued
- That the protocols for the three studies in Guinea need refinement
- That the proposed scientific working group be further discussed during the teleconference on Thursday.
That the idea of establishing small country groups, incorporating willing partners, was a good one that could serve, among other things, as an entry point for capturing government attention and engagement, and securing collaboration and approval as protocols evolve further.