Second teleconference on regulatory approaches for expediting development and availability of Ebola vaccines
27 January 2015, 15:00 – 16:00 (CET)

The second teleconference on regulatory approaches for expediting development and availability of Ebola vaccines was jointly chaired by Matthias Stahl and Mac Lumpkin.

Summary of the GSK vaccine Phase II CTA joint review meeting and the vaccine Phase III trials discussions in Geneva

An overview was given of two recent meetings at WHO: the joint review of the GSK Phase II vaccine trial application and discussions regarding Phase III clinical trials.

Highlights from the 15–16 December 2014 Joint Review of Phase II vaccine clinical trial application with Cameroon, Ghana, Mali, Nigeria, and Senegal for GSK’s Ebola vaccine. It was noted that following the AVAREF meeting in November and a request to WHO to convene a joint review, this was accomplished in a matter of weeks. This resulted in:

1. agreement on timelines for submission of additional information by by GSK to Regulatory and Ethics committees and for regulatory decision-making regarding the CTA;
2. use of an electronic platform for the first time for recording and responding to queries;
3. coordinated outcomes for the five countries
4. responses are currently being submitted and reviewed. Expect CTA authorization by end of February.

A Consultation on Phase III clinical trial designs was held on 17 December between the National Regulatory Authorities and Ethics Committees (NRAs and ECs) of Guinea, Liberia and Sierra Leone and partner institutions/sponsors (CDC, NIH, and WHO) planning Phase III clinical trials in those countries. Clinical trial designs for each country were presented to NRAs, ECs and vaccine manufacturers. Each plan and its timeline was discussed and the NRA raised requirements for regulatory compliance with each trial.

Update from GSK on their Phase II trial

An update on GSK’s progress since the December joint review was given and the current state of their vaccine trials was reported. The following has either been delivered or is underway:

1. The First set of additional requested information was submitted in mid-January, as agreed.
2. A second set of additional information has been delayed, but will include final dose selection (1 x 10^{11} viral particles), justification for dosage selection, Phase I safety and immunogenicity data, the pharmacy manual, and details of the final independent data monitoring committee. GMP certificates of analysis are still needed.
3. Plan on releasing vaccine for this trial end of February, with start of trial immediately thereafter, assuming all regulatory and ethics approvals final
4. Will need to focus now on importation of clinical trials supplies into the countries. WHO offered to help expedite. Next phone call between GSK and WHO will focus on this.
Updates on Phase III clinical trials

Liberia – US NIH
An update on Phase III clinical trial preparations was given. There was a brief discussion about the impact of declining EVD case numbers on the ability to go forward with the trial. The representative from NIH reported that operationally, they are ready to start the trial on 2 February. Authorization to conduct the trial has been received from the Liberian regulatory authorities.

Additionally, the Liberian – NIH team have responded to queries from US FDA and from the Liberian and US Ethics Committees and the committees have also given their approval. Approval from the US FDA is still pending, but was expected this week and if the approval is received the trial can start on 2 February.

Sierra Leone – US CDC
The representative from the US CDC provided an update on the joint Sierra Leone – CDC Phase III clinical trial. They are in the process of amending the trial design to accommodate the evolving epidemiology of the disease in Sierra Leone and have yet to select the vaccine that will be used. The pre-IND meeting with US FDA has been held and a plan has been made to submit the IND with a revised protocol to the US FDA and to the Pharmacy Board of Sierra Leone. It is hoped that enrolment in the trial can begin at the end of February.

Guinea – WHO
A WHO representative for the Guinea – WHO collaboration reported that a high-level WHO delegation was in Guinea this month and confirmed strong support from national authorities for the planned trial. Field visits have taken place and several sites have been identified as feasible.

Because WHO is the sponsor of this trial, it is not working directly with or providing support to national authorities on regulatory oversight issues to preclude even the appearance of a conflict of interest. Health Canada has agreed to a request from the Guinean authorities to provide regulatory support. A meeting between experts from Health Canada and Guinean regulatory authorities will take place 9-10 February in Paris to review the CTA. Regulatory documents are currently being translated into French and will be submitted to Guinean and Canadian authorities on 2 February. If all clearances are obtained, the trial should start on 28 February.

Both Merck and GSK vaccines will be used in trial, but will be administered sequentially. Which vaccine will be administered first has not yet been decided. An evidence-based algorithm, which is currently undergoing outside expert assessment, has been developed to aid in the selection. Authorization will be sought, in the initial CTA submission, to use both vaccines.

Update from a US FDA workshop on immunology of Ebola disease
On 12 December 2014, the US FDA hosted a workshop on immunology of Ebola disease, which was well-attended, both in person and via the Web. An in-depth discussion about primate immune markers (cellular and humoral) assay standardization needs was held during the workshop. Due to concerns that the incidence of disease may now be too low for trials to meet their effectiveness endpoints, there is a need for these markers and assays. Licensure may need to be based on those markers that are reasonably likely to predict clinical benefit.

Conclusions from the workshop included:
1. No single marker may be applicable for all vaccines.
2. Non-human primates appear to mimic human response, but the dose needed to achieve comparable levels in humans may be different.

A number of ideas were discussed: creating sample banks for use by various laboratories; forming a clinical assay working group; and further evaluation of humoral responses in human.

WHO reported that the UK’s NIBSC is working on standardization of reference antibodies and viral load RT-PCRs. A technical workshop will be held on 5–6 March 2015 to discuss these efforts.

**Update on WHO vaccine emergency use assessment and procurement listing procedure**

It was reported by WHO that the Organization is in the process of developing an emergency use assessment and listing procedure for vaccines. This is not a pre-qualification, but rather is a procedure to assess vaccine candidates for emergency use procurement listing in the context of a public health emergency of international concern.

The assessment document will address eligibility and minimal data requirements, but will maintain maximum flexibility to be able to address special needs of specific emergencies. The document is currently undergoing WHO internal clearance. Once cleared, it will be made public for community comments.

**WHO guidance to regulators on evaluation of products intended for use in public health emergencies of international concern**

At the request of certain Member States, WHO also is developing a guidance to help Member States that currently do not have national regulatory mechanisms to authorize vaccine clinical trials or vaccines use in the context of a public health emergency.

This document will discuss various types of regulatory procedures available for consideration for this purpose. It will also have a section that will specifically describe technical requirements for emergency authorization of Ebola vaccines in the context of a public health emergency. The first consultation on this document is planned for 19–20 March.

Having received reports from all participants, no further business was discussed.