The first teleconference on regulatory approaches for expediting development and availability of Ebola vaccines was chaired by the Assistant Director-General, Dr Marie-Paule Kieny.

Dr Kieny welcomed the 48 participants on the call and explained that the teleconference was set up with the following objectives:

1) to review the critical regulatory paths for the lead candidate Ebola vaccines and identify the main regulatory challenges;

2) to clarify the timelines for availability of these vaccines for both clinical trials and potential future large-scale deployment;

3) to discuss and map out possible avenues to address the regulatory challenges while keeping safety as a main concern.

In preparation for the teleconference, two manufacturers, GSK and J&J, provided the WHO Secretariat with, respectively, a mapping of their critical regulatory path and a concept note on proposed strategies to address regulatory challenges. Dr Kieny commended GSK for being very transparent in sharing their detailed critical path plan for Ebola vaccine development. On behalf of WHO, she assured participants that WHO will do all to facilitate the development and regulatory evaluation of Ebola vaccines to avoid any delay. Following the introductory remarks, representatives of GSK, Newlink and J&J briefly presented their plans for Ebola vaccine development.

**GSK:**

The critical path plan that was provided was briefly described. The company’s main goal is to ensure that vaccine doses will be available for use by mid-January 2015 at the latest. Taking into consideration the fact that many steps are not completely under the control of the company, GSK estimates around a 50% chance to complete the plan according to the timetable. Submission of a data package requesting advice to both US FDA and EMA on 7th November 2014 is seen as an important next step in the overall vaccine evaluation process.

Representatives of US FDA and EMA thanked GSK for being very transparent and expressed their strong commitment and flexibility to review the data as rapidly as possible. Both agencies are prepared to discuss and solve problems through bilateral discussion with the manufacturer in real time in the interest of global public health.

Comments from Paul-Ehrlich Institute addressed the rapidity of expected decision making once phase I data are available, and the importance of integrating African regulators in the discussion.

**NewLink:**

The company is planning to start a phase II study in December. They requested that WHO and AVAREF support the company to obtain import permits for the investigational product. It is clear that the timeline for integrating immunogenicity and safety data from African trials is very tight and
this is one of the uncertainties that NewLink is working with in terms of availability of doses for larger scale use.

Proposal from the Paul-Ehrlich Institute was to explore whether scientific advice from US FDA and from EMA could be jointly issued.

J&J:

The company is not yet in a position to provide the same level of details as GSK but is also aiming for submission of data to EMA and US FDA for scientific opinion/advice. Potential challenges are similar to those reported by GSK such as criteria and timelines for vaccine lot release and also included limited access to BSL2 filling facilities. The company will make the scientific case that animal and human data generated from vaccines derived from the same vector-based platforms but encoding non-Ebola related inserts, as well as those expressing the same Ebola insert in related platforms, could be considered in order to accelerate timelines for regulatory approval of clinical trials. This analysis will be presented to the regulators. Biosafety requirements for the non-replicating component of the vaccine candidate, as well as bridging studies from animals to humans for immunogenicity as a basis for initiating efficacy studies are critical regulatory issues that need to be resolved.

EMA commented that immunogenicity bridging from animals to humans is an issue on which an international consensus would be needed.

Discussion

Both regulators and manufacturers expressed their willingness to ensure that the review process will be efficient as possible in the interest of global public health. There are two types of questions to be addressed: 1) general scientific questions that will impact the regulatory process and 2) specific questions related to manufacturing, nonclinical and clinical evaluation of specific products. The issue of bridging immunogenicity from animals to humans is an example of a general scientific issue that could be addressed by an expert group. In this context, FDA announced that it is planning a public workshop in December on the “Immunology of protection from Ebola virus infection”. FDA invited participants to the call to join this consultation. WHO offered to facilitate meetings on regulatory science issues that would benefit from input from the international scientific community.

The representative of the US FDA announced that trilateral calls between FDA-EMA-Health Canada on specific Ebola vaccine issues have been happening on a regular basis and that these would be extended, under appropriate confidentiality agreements, to include other regulators and WHO.

Dr Wood explained that the African Vaccine Regulatory Forum (AVAREF) provides a platform for African regulators and members of national Ethical Committees to discuss issues of common interest. The next AVAREF meeting will take place in the week of 3rd November and will be a key opportunity to engage regulators from the continent on issues regarding Ebola vaccines. Dr Akanmori added that one of AVAREF’s planned activities is to organize joint regulatory reviews of Ebola vaccine dossiers as a technical assistance to countries.
Next steps

Dr Kieny concluded the discussion, recalling the request by FDA and EMA that product-specific related issues should be addressed by regulators and manufacturers on a bilateral basis, and taking note of the willingness of regulators to make such processes as efficient as possible.

Below is a summary of action points that were agreed in the call:

- Broader multilateral teleconferences will be organized among regulators to discuss product-specific issues under confidentiality agreement. These calls will include WHO;
- Invitations will be extended by FDA to interested parties to a public workshop on “Immunology of protection from Ebola virus infection”;
- Additional regulatory science topics on Ebola vaccines will be identified for follow-up;
- Monthly calls will be organized by WHO and will focus on (a) general progress against the timelines for vaccine availability and (b) report back on progress in resolving scientific issues that impact regulatory decisions.