Terms of reference for the EMA/HC/FDA cluster on Vaccines

European Medicines Agency (EMA), Health Canada (HC) and US Food and Drug Administration (FDA) agree on the following:

1. Objectives and goals

The EMA/HC/FDA cluster on Vaccines should fulfil the following objectives:

- Discuss the evidentiary basis, regulatory context, and scientific rationale for each Agency's approach to specific issues in vaccine development and licensure, with the goal of reaching a thorough understanding of each Agency's positions, and where possible, achieving convergent views.
- Provide a forum for discussion of candidate vaccines and vaccine classes including issues such as:
  - regulatory pathways
  - pre-clinical evidence to support development programs
  - clinical trial design including trial end points and statistical analyses
  - novel/alternative approaches to accruing data to support regulatory decision-making (e.g., biomarkers, "real world evidence", and decentralized clinical trials)
  - clinical safety evaluation
  - labelling aspects
  - post marketing monitoring of vaccine safety and effectiveness
  - as needed, issues related to manufacturing process and controls (excluding trade secret information)
- Offer a confidential forum for exchange of draft documents, policies in development, updates regarding workshops and public hearings, and more detailed information supporting the scientific basis for decision making.
- Address new issues and ensure a global discussion for novel vaccines including those developed to prevent emerging pathogens through confidential sharing of reports. The primary goal of this cluster is to share scientific evaluation of various aspects of vaccine development for infectious diseases. These aspects include investigation of the immune response, vaccine dose and schedule selection, clinical trials design including trial end points and target populations, opportunities for regulatory flexibility (approval supported by other than two adequate and well controlled studies and/or use of immune markers as surrogate endpoints including options for immuno-bridging), determination of safety, evaluation of pre-clinical data needed to support human trials, and design and conduct of post-marketing studies .The main mechanism to achieve these goals will be regularly scheduled teleconferences, including individuals from review divisions and therapeutic teams, for exchange of information and experiences.

It may be appropriate to agree to additional in-depth discussions on specific topics during separate ad hoc teleconferences when it might be relevant to include participation of appropriate EMA/HC/FDA staff members.

Cluster participants will discuss and determine which topics will be discussed at this cluster and which will be deferred to other platforms/clusters, e.g. Paediatric, Pharmacovigilance related topics. When topics are deferred to other platforms/clusters, a summary of discussions will be reported back to this cluster.

2. Participants

From the EMA side, participants will include EMA staff members (from Anti-infective and Vaccine, Public Health Threats Office, who will also be providing the cluster secretariat, Vaccines and therapies for infectious diseases, Paediatric medicines, Regulatory Affairs, Quality Office, Scientific Advice, and International Affairs), Emergency Task Force (EFT) members and NCA assessors from the Vaccine Working Party. In addition, depending on the topic and issue to be discussed, participants will include colleagues from other teams (Specialised Division), Statistics and EU assessors from other committee (e.g. CHMP or PDCO) or working party members (e.g. BWP), as appropriate.

FDA will involve colleagues from the Center for Biologics Evaluation and Research (CBER) including the Office of Vaccines Research and Review (OVRR), the Office of Center Director, the Office of Biostatistics and Pharmacovigilance (OBPV), the Office of Compliance and Biologics Quality (OCBQ), and the Office of Global Policy and Strategy, Europe Office ,and in some cases, review staff and/or management from other Centers in the Agency (e.g., CDER, CDRH).

Health Canada participants will include Biologic and Radiopharmaceutical Drugs Directorate (BRDD), including the, Centre for Vaccines, Clinical Trials and Biostatistics, Office of Regulatory Affairs, Centre for Policy, Pediatrics and International Collaboration and the Marketed Health Products Directorate (MHPD) and other Vaccine subject matter experts, as appropriate.

The teleconferences will be chaired by the three Agencies in a rota system with acting chair responsibilities alternating at sequential meetings. High level minutes and action lists will be drafted by the Agency chairing the meeting and will be circulated to the other Agencies for comments within three weeks from the day of the meeting.

EMA, HC, and FDA agree that observers from regulatory authorities of other regions may participate in cluster activities subject to agreement of the EMA, HC, and FDA and appropriate confidentiality arrangements being in place.

3. Timing

It is anticipated that teleconferences will occur three times per year, subject to need and predefined in advance, and each meeting to be conducted for up to 2 hours.

Ad-hoc teleconferences, on product-related assessments or any other emerging concerns, of a more pressing nature can be held at any mutually agreeable time. As appropriate, some discussions will be moved to other clusters to expedite review.

4. Working arrangements

EMA, HC, and FDA will alternate the responsibility to prepare teleconference agendas, including mutually agreed topics for discussion in alignment with the objectives described under section 1. The topics should be selected based on shared interests and are anticipated to be beneficial for all three agencies. Liaisons will play an administrative role in assigning topics to avoid duplication of efforts.

A proposed draft agenda conforming to the template will be sent by the organising Agency about one week in advance of a teleconference; however proposals should be circulated via email at least 3 weeks in advance to verify topic for mutual agreement. Urgent topics may be added shortly before the teleconference by mutual agreement.

Once the agenda has been agreed upon, the need for additional ad hoc teleconferences may be identified for in-depth discussion of specific issues, and a specific agenda for such ad hoc teleconferences will be set. Attendees for these ad hoc meetings will be limited to those actively working on the topic, subject matter experts and core Cluster members as needed.

5. Confidentiality

Confidentiality of the information shared within the cluster is covered under the bilateral information sharing Confidentiality Arrangements (CA) that exist between members and observers. Cluster members and observers are responsible for the implementation and maintenance of these arrangements.

Cluster members, as well as observers and guests, shall not disclose publicly or do anything that would lead to the disclosure of information shared or discussed during meetings without prior authorization of the members that provide such information.

The chairs will inform meeting attendees if there are participants from outside of member or permanent observer organizations.

6. Reaching Agreement

The cluster will come to final decisions using the process of consensus, defined as general verbal agreement, to the greatest extent possible.

7. Workplan and Reporting

No specific document other than agendas, high level summary of the discussion per topic and agreed upon action points will be routinely generated, although cluster members may decide to create documents that may be shared, as appropriate, with other clusters. The teleconferences may be supported by already existing EMA, HC or FDA documents.

A joint bi-annual workplan outlining the cluster's priorities is generated and routinely supported by actions. A report highlighting the activities of the cluster will be prepared with a specified frequency.

Under the confidentiality agreement, records relevant to specific discussion topics (such as clinical protocols, study reports, and minutes from sponsor meetings or Scientific Advice interactions) may be exchanged before or after cluster meetings in order to enable efficient discussion and comprehensive understanding of the issues