EMA/410493/2019

Terms of reference for the EMA/FDA cardiovascular cluster

The European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) agree on the following:

1. Goals and Objectives

The primary goal of the cardiovascular cluster is to share scientific evaluation of various aspects of drug development for cardiovascular diseases. The following objectives are defined:

- Achieve a common understanding of each Agency's regulatory approaches to cardiovascular diseases drug development as based on internal policies, guidance documents and regulations.
- Provide a forum for discussion during the evaluation phase of candidate drugs and drug classes for the treatment of cardiovascular diseases including issues such as:
    - trial end points
    - safety populations
    - statistical approaches to cardiovascular diseases populations
    - methodologies for post marketing issues
    - pre-clinical evidence to support development programs
    - as needed, issues related to chemistry, manufacturing and controls (excluding trade secret information).
- Provide a forum for discussion of post-marketing topics for medicines treating CV diseases such as (emerging) safety concerns, extension applications
- Offer a confidential forum for exchange of draft documents, guidelines in development, and more detailed information supporting the scientific basis for decision making
- Establish ad hoc and systematic exchange of information for the benefit of both entities.
- Address long term safety issues and ensure a global safety net for drugs developed in the cardiovascular area through confidential sharing of reports.

To achieve these objectives regular teleconferences, for exchange of information and experiences, will be scheduled (around 4 meetings/year). In addition, ad-hoc exchanges to obtain (rapid)

information are also foreseen in the form of written exchanges but as well ad-hoc teleconferences can be organised on an as needed basis. The work of the cluster is conducted within the confidentiality arrangements in place between the participating parties.

2. Participants

From the EMA side, participants will include EMA staff members from the Office for Therapies for Endocrine and Cardiovascular Diseases (H-ECV) and from the Scientific Advice office. Other EMA participants can be included depending on the topic. Concerned rapporteurs and assessors and other committee or Cardiovascular Working Party members will be invited, as appropriate.

The FDA will include staff from the Division of Cardiovascular and Nephrology (DCN).

EMA and FDA international liaisons will also be included.

The teleconferences will be co-chaired by the EMA (H-ECV) and the FDA (DCN). Acting chair responsibilities are reviewed and agreed annually.

Health Canada and Swissmedic are permanent observers of the cardiovascular cluster.

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

3. Timing

It is anticipated that teleconferences will occur quarterly, subject to need and predefined in advance, each meeting to be conducted for approximately 1 hour.

Ad-hoc teleconferences, on product-related assessments, 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.

For some specific cardiovascular topics, it might be more appropriate to organise specific teleconferences with specific experts.

4. Agenda setting

The EMA and the FDA will share 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 on the grounds that they are of shared interest and provide useful insight

on medicines in development, ongoing evaluations of medicines under the cardiovascular therapeutic area and general cardiovascular topics. A proposed draft agenda will be sent by either the EMA or the FDA in advance of a teleconference to verify topic proposals for mutual agreement. The final agenda should be available two weeks before the teleconference. Urgent topics may be added shortly before the teleconference by mutual agreement.

5. Records and supporting documents

No specific document other than agendas and agreed upon action points will be routinely generated, although cluster member may decide to create documents that may be shared, as appropriate, with other clusters. The teleconferences may be supported by already existing EMA or FDA documents.

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