ICH E14/S7B IWG Work Plan
July 31, 2019

Topic Adoption date: *November 2018*

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Last Face-to-Face Meeting: *Amsterdam, the Netherlands – June 2019*

1. Key milestones

1.a. Current status of key milestones

Past completion date	Milestone
Dec. 2015	*Finalized E14 Q&A regarding concentration-QTc analysis as an alternative analysis endpoint for QTc evaluation.*
Dec. 2017	*Publication of a white paper article to describe in more detail the steps involved in appropriate concentration-QTc analysis.* *(https://doi.org/10.1007/s10928-017-9558-5)*
June 2018	*A recommendation (a concept paper proposed through FDA) to ICH Assembly to reconstitute a WG at this time for the ICH E14 / S7B topic for clarification of the ICH S7B guideline through Q&As.*
Aug. 2018	*Revised concept paper for submission to the MC.*
Nov. 2018	*E14/S7B Discussion Group (DG) met in person and revised the concept paper to develop Q&As to both ICH S7B and E14. The concept paper describes a two-stage approach where Q&As will be written for both S7B and E14 in each stage. The concept paper was endorsed by the ICH Assembly and an Implementation Working Group (IWG) was formed.*
June 2019	*E14/S7B IWG met in person and discussed draft Q&As for stage 1. The draft Q&As for best practice for in vitro and in vivo studies and principles for proarrhythmia models reached general consensus. A decision was made to split the integrated risk assessment Q&A into two parts, one for S7B and one for E14. The discussion of stage 2 Q&A was also started.*

1.b. Future anticipated key milestones

Expected future completion date	Milestone
June 2020	*Steps 3 and 4 for first stage Q&As for ICH S7B and E14*

2. Timeline for specific tasks

Beginning date	End date	Task / Activity	Details
Nov. 2018	*Nov. 2018*	*Create Concept Paper for MC and Assembly*	*Create Concept Paper regarding updating ICH E14 and S7B with Q&As. Develop work plan.*
Nov. 2018	*Nov. 2018*	*Finalize Concept Paper and work plan for IWG*	*Finalize a detailed plan on the timelines to write the proposed Q&As for S7B and E14.*
Dec. 2018	*June 2019*	*Scope first stage Q&As for S7B and E14 and develop draft text*	*In regular teleconferences discuss scope and detail of potential Q&As for ICH S7B and E14.*
Dec. 2018	*Jan. 2019*	*Establish six sub-groups to discuss specific topics and draft Q&As*	*Establish four sub-groups to draft stage 1 Q&As (Best practices for in vitro assay; Considerations for S7B in vivo core battery assay; Principles for proarrhythmia models; Integrated risk assessment that combines S7B & E14). Establish two sub-groups to discuss related topics (Additional drugs/data required for advancing Stage 2; Large molecule threshold)*
June 2019	*June 2019*	*Meet face-to-face at ICH Meeting*	*Discuss the potential Q&As on best practices for ICH S7B assays, and criteria for robust proarrhythmia prediction model. Discuss the potential Q&As for E14 in clinical implementation scenarios.*

June 2019	*November 2019*		• *Reach agreement on best practice and proarrhythmia models stage 1 Q&As for regions to seek internal feedback from constituencies* • *Incorporate constituency feedback to finalize Q&As* • *Draft Integrated Risk Assessment Q&A for S7B and revisions to E14 Q&As*
November 2019	*November 2019*	*Meet face-to-face at ICH Meeting*	• *Meet face-to-face to finalize in vitro & in vivo best practice and proarrhythmia models Q&As* • *Seek consensus on Integrated Risk Assessment Q&A for S7B and revisions to E14 Q&As* • *Discuss second stage Q&As*
November 2019	*June 2020*	*Incorporate constituency feedback on stage 1 Q&As*	*Incorporate constituency feedback on Integrated Risk Assessment Q&A for S7B and revisions to E14 Q&As*
June 2020	*June 2020*	*Stage 1 Q&A sign off and discuss stage 2 Q&A*	• *Meet face-to-face for step 1 sign-off of first stage Q&As* • *Discuss second stage Q&As and finalize timeline*
Jan. 2019	*June 2020*	*Discuss potential second stage Q&As for S7B and E14 and generate any data needed*	*In regular teleconferences discuss the potential second stage Q&As focusing on data needs and gaps. In face-to-face meetings discuss data needs and timelines. A detailed timeline to finalize Q&As will be developed.*