ICH E14/S7B IWG Work Plan
20 February 2019

Topic Adoption date: *15 November 2018*

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Last Face-to-Face Meeting: *Charlotte, NC, USA – November 2018*

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.*

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	*June 2020*	*Finalize first stage Q&As for S7B and E14*	*In regular teleconferences draft the Q&A text in preparation for the face-to-face meeting and Q&A finalization.*
June 2020	*June 2020*	*Meet face-to-face at ICH Meeting*	*Finalize first stage Q&As.*

Jan. 2020	*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.*