ICH E14/S7B Implementation Working Group Work Plan
February 15, 2022

Topic Adoption date: *15 November 2018*

Rapporteur: *Dr. David Strauss - FDA, United States*

Regulatory Chair: *none*

Last Face-to-Face Meeting: *Singapore – November 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)*
Jun. 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.*
Jun. 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.*
Nov. 2019	*E14/S7B IWG met in person again to discuss stage 1 Q&A. The draft Q&As for best practice for in vitro and in vivo studies and principles for proarrhythmia models were edited based on constituency feedback. A general consensus was reached for the S7B Integrated Risk assessment Q&A. Significant progress was made to reach a consensus on the E14*

	Integrated Risk Assessment Q&A. Potential stage 2 Q&A and data needs were also discussed.
Jul. 2020	*Step 1 sign-off for the first stage Q&As for ICH E14 and S7B was completed*
Aug. 2020	*Step 2a confirmation of consensus of the Technical Document and Step 2b adoption of the Draft Guideline for the first stage Q&As for ICH E14 and S7B was completed*
Oct. 2020	*A public webinar was held to provide an overview of Draft Guideline Q&As to E14 and S7B and answer/discuss questions received during the webinar*
Dec. 2020	*Step 3, i) Regional regulatory consultation was completed (end of public consultation period for the first stage Q&As)*
Jul. 2021	*Step 3, ii) All regional consultation comments have been discussed and a revised version of the Step 2b Final Draft Guideline has been developed that is still being discussed/reviewed by the IWG.*
Jan. 2022	*Step 3 sign-off*
Feb. 2022	*Step 4 adoption*

1.b. Future anticipated key milestones

Expected future completion date	Milestone
Nov. 2021 – Feb. 2022	*Develop initial technical training material that will be released together with the Step 4 document of the first stage Q&As*
Nov. 2021 – Jun. 2022	*Develop more comprehensive technical training material for first stage Q&As and timeline/recommendation for second stage Q&As*

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	*Jun. 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)*
Jun. 2019	*Jun. 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.*
Jun. 2019	*Nov. 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*
Nov. 2019	*Nov. 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*

Nov. 2019	*Jun. 2020*	*Incorporate constituency feedback on stage 1 Q&As*	*Incorporate constituency feedback on In Vitro, In Vivo, Principles for Proarrhythmia Models, and Integrated Risk Assessment Q&A for S7B. Make revisions and incorporate constituency feedback to E14 Q&As*
Jun. 2020	*Jul. 2020*	*Stage 1 Q&A sign off*	• *Step 1 sign-off for first stage Q&As*
Jun. 2020	*Aug. 2020*	*Step 2a/2b endorsement of stage 1 Q&As*	• *Step 2a/2b endorsement of the draft Q&As for stage 1*
Jul. 2020	*Nov. 2020*	*In preparation for the public consultation/public meeting*	• *All regions make procedure preparations for their public consultation periods* • *Plan and execute virtual public meeting (webinar) to disseminate the concepts behind the draft Q&As*
Jul. 2020	*Dec. 2020*	*Step 3 regional consultation*	• *Public comment received from respective regions*
Jan. 2021	*Oct. 2021*	*Step 3 discussion of regional comments*	• *Finalize and sign off the first stage Q&As* • *Develop of training materials to support the implementation of guidelines*
Oct. 2021	*Jan. 2021*	*Step 3 experts sign-off by the regulatory experts*	• *Reach consensus on a revised version of the Step 2B Final Draft Guideline for sign-off by the regulatory experts*
Dec. 2021	*Feb. 2022*	*Step 4 adoption of the first stage Q&As*	• *Step 4 adoption of the harmonized Guideline for the Regulatory Members of the Assembly*

Nov. 2021	*Feb. 2022*	*Develop and finalize initial training material*	• *Complete and finalize initial training material for dissemination on ICH website together with the step 4 document*
Nov. 2021	*Jun. 2022*	*Develop and finalize comprehensive training material*	• *Complete and finalize comprehensive training material for dissemination on ICH website after the release of the step 4 document*
Jan. 2019	*~Jan.-Jun. 2022*	*Discuss potential second stage Q&As for S7B and E14 and make recommendation for data needs for second stage Q&As*	*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. Finalize timeline and/or recommendations for data needs for second stage Q&As.*
Jun. 2022	*Sep. 2022*	*Disseminate comprehensive training material for stage 1 Q&As*	*Following professional production of the comprehensive training material, it will be disseminated on the ICH website for the first stage Q&As*