

# ICH E14/S7B IWG Work Plan

## September 15, 2020

**Topic Adoption date:** 15 November 2018

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**Regulatory Chair:** N/A

**Last Face-to-Face Meeting:** Singapore – November 2019

### 1. Key milestones

#### 1.a. Current status of key milestones

Past completion date	Milestone
<b>Dec. 2015</b>	<i>Finalized E14 Q&amp;A regarding concentration-QTc analysis as an alternative analysis endpoint for QTc evaluation.</i>
<b>Dec. 2017</b>	<i>Publication of a white paper article to describe in more detail the steps involved in appropriate concentration-QTc analysis. (<a href="https://doi.org/10.1007/s10928-017-9558-5">https://doi.org/10.1007/s10928-017-9558-5</a>)</i>
<b>June 2018</b>	<i>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&amp;As.</i>
<b>Aug. 2018</b>	<i>Revised concept paper for submission to the MC.</i>
<b>Nov. 2018</b>	<i>E14/S7B Discussion Group (DG) met in person and revised the concept paper to develop Q&amp;As to both ICH S7B and E14. The concept paper describes a two-stage approach where Q&amp;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.</i>
<b>June 2019</b>	<i>E14/S7B IWG met in person and discussed draft Q&amp;As for stage 1. The draft Q&amp;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&amp;A into two parts, one for S7B and one for E14. The discussion of stage 2 Q&amp;A was also started.</i>
<b>Nov. 2019</b>	<i>E14/S7B IWG met in person again to discuss stage 1 Q&amp;A. The draft Q&amp;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&amp;A. Significant progress was made to reach a consensus on the E14</i>

	<i>Integrated Risk Assessment Q&amp;A. Potential stage 2 Q&amp;A and data needs were also discussed.</i>
<b>July 2020</b>	<i>Step 1 sign-off for the first stage Q&amp;As for ICH E14 and S7B was completed</i>
<b>Aug. 2020</b>	<i>Step 2a confirmation of consensus of the Technical Document and Step 2b adoption of the Draft Guideline for the first stage Q&amp;As for ICH E14 and S7B was completed</i>

### 1.b. Future anticipated key milestones

<b>Expected future completion date</b>	<b>Milestone</b>
<b>15-16, Oct 2020</b>	<i>Public webinar to provide an overview of Draft Guideline Q&amp;As to E14 and S7B and answer/discuss questions received during the webinar</i>
<b>Jan 2021</b>	<i>Step 3 end of public consultation period for the first stage Q&amp;As</i>
<b>June 2021</b>	<i>Meet in person for Step 3 signoff</i>
<b>July 2021</b>	<i>Step 4 adoption of the first stage Q&amp;As</i>
<b>Nov 2021</b>	<i>Meet in person to finalize technical training material for first stage Q&amp;As and discuss timeline/recommendation for second stage Q&amp;As</i>
<b>Jan 2022</b>	<i>Disseminate training material on ICH website for first stage Q&amp;As and timeline/recommendation for second stage Q&amp;As</i>

### 2. Timeline for specific tasks

<b>Beginning date</b>	<b>End date</b>	<b>Task / Activity</b>	<b>Details</b>
<b>Nov. 2018</b>	<i>Nov. 2018</i>	<i>Create Concept Paper for MC and Assembly</i>	<i>Create Concept Paper regarding updating ICH E14 and S7B with Q&amp;As. Develop work plan.</i>
<b>Nov. 2018</b>	<i>Nov. 2018</i>	<i>Finalize Concept Paper and work plan for IWG</i>	<i>Finalize a detailed plan on the timelines to write the proposed Q&amp;As for S7B and E14.</i>
<b>Dec. 2018</b>	<i>June 2019</i>	<i>Scope first stage Q&amp;As for S7B and E14 and develop draft text</i>	<i>In regular teleconferences discuss scope and detail of potential Q&amp;As for ICH S7B and E14.</i>
<b>Dec. 2018</b>	<i>Jan. 2019</i>	<i>Establish six sub-groups to discuss specific topics and draft Q&amp;As</i>	<i>Establish four sub-groups to draft stage 1 Q&amp;As (Best practices for in vitro assay; Considerations for S7B</i>

			<i>in vivo core battery assay; Principles for proarrhythmia models; Integrated risk assessment that combines S7B &amp; E14). Establish two sub-groups to discuss related topics (Additional drugs/data required for advancing Stage 2; Large molecule threshold)</i>
<b>June 2019</b>	<i>June 2019</i>	<i>Meet face-to-face at ICH Meeting</i>	<i>Discuss the potential Q&amp;As on best practices for ICH S7B assays, and criteria for robust proarrhythmia prediction model. Discuss the potential Q&amp;As for E14 in clinical implementation scenarios.</i>
<b>June 2019</b>	<i>November 2019</i>		<ul style="list-style-type: none"> <li>• <i>Reach agreement on best practice and proarrhythmia models stage 1 Q&amp;As for regions to seek internal feedback from constituencies</i></li> <li>• <i>Incorporate constituency feedback to finalize Q&amp;As</i></li> <li>• <i>Draft Integrated Risk Assessment Q&amp;A for S7B and revisions to E14 Q&amp;As</i></li> </ul>
<b>November 2019</b>	<i>November 2019</i>	<i>Meet face-to-face at ICH Meeting</i>	<ul style="list-style-type: none"> <li>• <i>Meet face-to-face to finalize in vitro &amp; in vivo best practice and proarrhythmia models Q&amp;As</i></li> <li>• <i>Seek consensus on Integrated Risk Assessment Q&amp;A for S7B and revisions to E14 Q&amp;As</i></li> <li>• <i>Discuss second stage Q&amp;As</i></li> </ul>
<b>November 2019</b>	<i>June 2020</i>	<i>Incorporate constituency feedback on stage 1 Q&amp;As</i>	<i>Incorporate constituency feedback on In Vitro, In Vivo, Principles for Proarrhythmia Models, and Integrated Risk Assessment Q&amp;A for S7B. Make revisions and incorporate constituency feedback to E14 Q&amp;As</i>

<b>June 2020</b>	July 2020	Stage 1 Q&A sign off	<ul style="list-style-type: none"> <li>• Step 1 sign-off for first stage Q&amp;As</li> </ul>
<b>June 2020</b>	Aug 2020	Step 2a/2b endorsement of stage 1 Q&As	<ul style="list-style-type: none"> <li>• Step 2a/2b endorsement of the draft Q&amp;As for stage 1</li> </ul>
<b>July 2020</b>	Nov 2020	In preparation for the public consultation/public meeting	<ul style="list-style-type: none"> <li>• All regions make procedure preparations for their public consultation periods</li> <li>• Plan and execute virtual public meeting (webinar) to disseminate the concepts behind the draft Q&amp;As</li> </ul>
<b>July 2020</b>	Dec 2020	Step 3 regional consultation	<ul style="list-style-type: none"> <li>• Public comment received from respective regions</li> </ul>
<b>Jan. 2021</b>	June 2021	Step 3 discussion of regional comments	<ul style="list-style-type: none"> <li>• Finalize and sign off the first stage Q&amp;As</li> <li>• Development of training materials to support the implementation of guidelines</li> </ul>
<b>June 2021</b>	June 2021	Step 3 experts sign-off by the regulatory experts	<ul style="list-style-type: none"> <li>• Meet face-to-face for reaching consensus on a revised version of the Step 2B Final Draft Guideline</li> </ul>
<b>June 2021</b>	January 2022	Complete and finalize training material	<ul style="list-style-type: none"> <li>• Complete and finalize training material for dissemination on ICH website</li> </ul>
<b>Nov 2021</b>	Nov 2021	Finalize technical training material and discuss 2 <sup>nd</sup> stage Q&As	<ul style="list-style-type: none"> <li>• Meet face-to-face to finalize technical training material (voice-over slide set) to be sent for production and discuss timeline/recommendation for second stage Q&amp;As</li> </ul>
<b>Jan. 2019</b>	Dec 2021	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

			<i>needs and timelines. Finalize timeline and/or recommendations for data needs for second stage Q&amp;As.</i>
<b>Jan. 2022</b>	<i>Jan. 2020</i>	<i>Disseminate training material for stage 1 and timeline/recommendation for stage 2</i>	<i>Disseminate training material on ICH website for first stage Q&amp;As and timeline/recommendation for second stage Q&amp;As</i>