ICH
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ICH Q1: Stability Testing of Drug Substances and Drug Products

Step 2 document – to be released for comments 11 April 2025

International Council for Harmonisation of Technical Requirements
for Pharmaceuticals for Human Use

Legal Notice

History

- **This document has been signed off as a *Step 2* document (11 April 2025) to be issued by the ICH Regulatory Members for public consultation**
- **This document was developed based on a Concept Paper (15 November 2022) and a Business Plan (15 November 2022)**

Outline

These slides are intended to orient the reader/commentor with the revised stability guideline and provide guidance on commenting. The slides are organised as follows:

- Background on Revision
- Milestones
- Key Considerations
- Recommendations for Guideline Review
- Table of Contents for Draft Technical Document
- Summary of Draft Guideline Content
- Recommendations for Commenting
- Instructions for Commenting

Background on Revision

Revision of the ICH Stability Guideline Series Q1A-F and Q5C was recommended to:

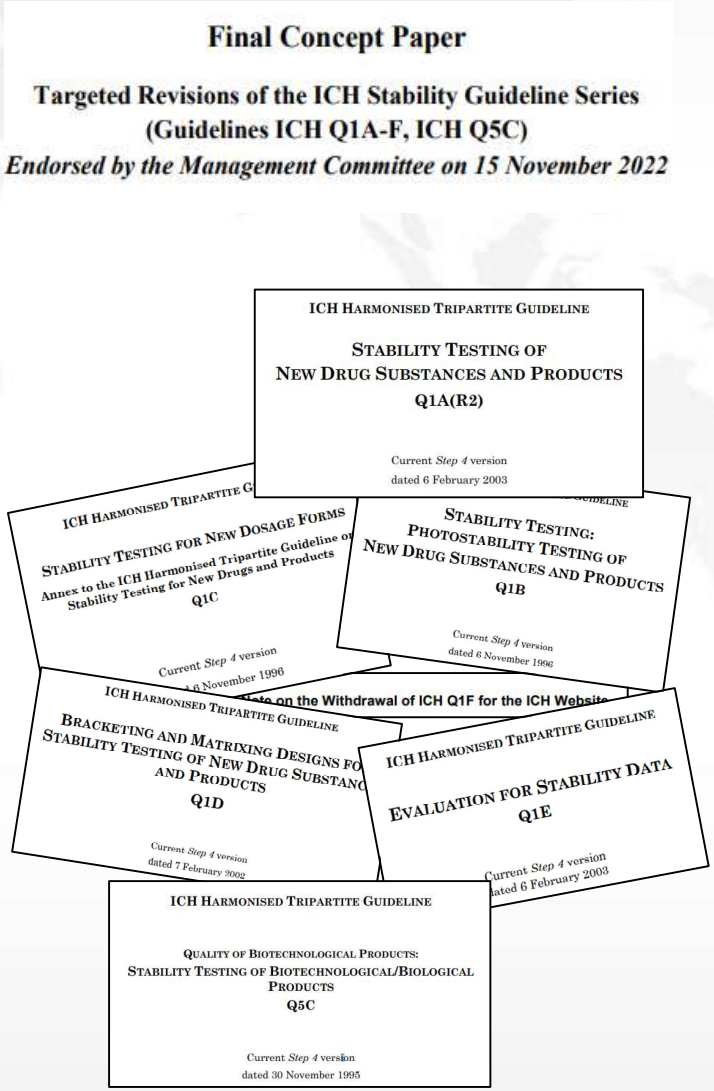
a) Streamline the series by combining the various guidelines into a single guideline focused on core stability principles;

b) Promote harmonised interpretation by addressing potential gaps and areas of ambiguity;

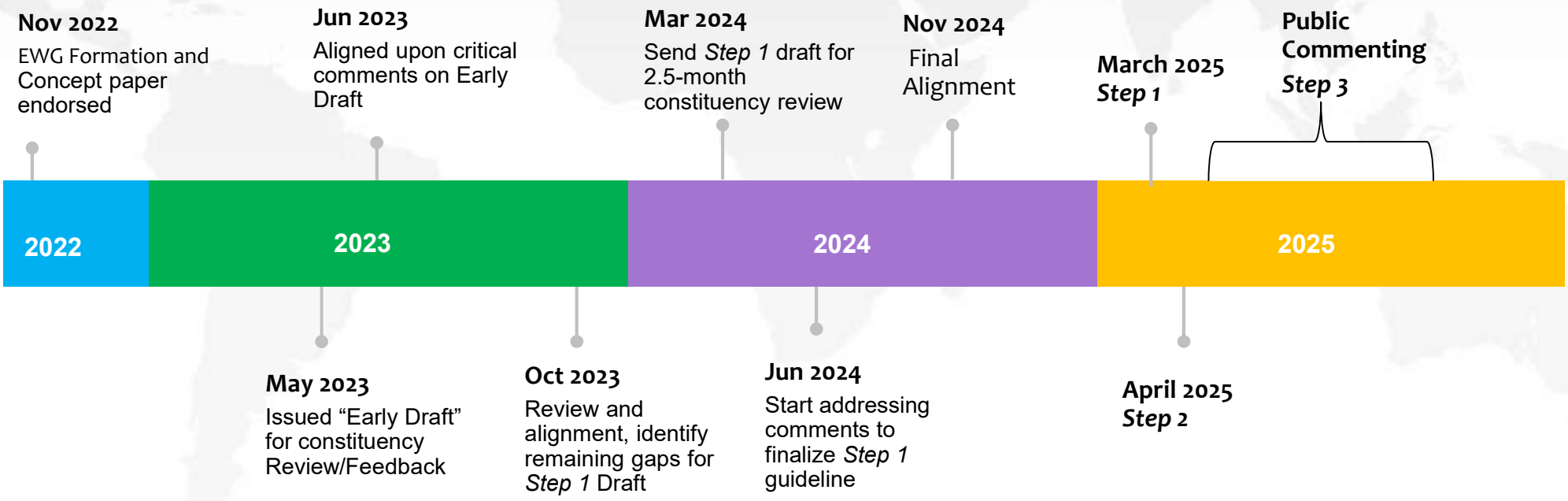
c) Address additional technical issues, including relevant stability strategies and innovative tools that strengthen the application of risk management;

d) Consider inclusion of new topics, such as stability considerations for advanced therapies.

The result will be a combined guideline, ICH Q1, with integrated annexes that address specific topics beyond the core principles on stability recommendations and to address product type specific recommendations.



ICH Q1 Revision Milestones



Note: The *Step 2* document is a draft Guideline for public comment. Revisions will occur based on public commenting.

The document will undergo changes through *Step 4* and should not be used or referenced as the final Guideline.

Key Considerations

The Q1 Draft Guideline:

- combines and modernizes the content of ICH Q1A-F series and ICH Q5C into one comprehensive stability guideline, addressing a range of product types
- should be considered in its entirety for a comprehensive approach to stability studies
- exemplifies the standard stability data package for regulatory submission for a range of product types and includes recommendations for studies managed within the Pharmaceutical Quality System (PQS)
- provides new content (e.g., in-use studies, short-term stability studies, processing and holding times, adjuvant and reference standard studies, product lifecycle and modelling)
- enables science- and risk-based approaches and addresses new technologies and modern strategies as part of enhanced product understanding

Recommendations for Draft Guideline Review

Read the entire Draft Guideline. The EWG recommends that reviewers read the Draft Guideline in its entirety before providing detailed comments. The organisation of this guideline is different from the existing ICH stability guidelines. Content that may initially appear to be missing may be provided in a different section.

Keep guideline scope in mind. The scope of product types that this Draft Guideline covers is broad. Guidance on all product-specific scenarios cannot be provided within the guideline.

The guideline exemplifies the standard approach, **with strategies for alternative approaches**. The core Draft Guideline focuses on assessing product stability using the concepts established within the ICH Q1 series and ICH Q5C. Alternative approaches may be applied to any part of the guideline, when scientifically justified.

Recognise that enhanced stability modelling is an evolving space. The guidance on this topic is written to enable application of current tools and future advancements.

ICH Q1 *Step 2* Draft Guideline - Table of Contents

Summary of ICH Q1 Draft Guideline Content

- ***Section 1*** provides an introduction and is important for understanding the scope of this guideline and how it differs in format from existing stability guidelines. It is recommended to read this section first and refer to it as needed throughout the guideline review.
- ***Section 2*** provides guidance on how data that is often generated early in development (e.g., to understand intrinsic stability, potential degradation products/pathways, confirm method suitability, and enable method validation) may be used to inform stability protocol design and support long term storage. This section aims to consolidate content on stressed stability and forced degradation currently existing in ICH Q1A and/or ICH Q5C.

Summary of ICH Q1 Draft Guideline Content

- ***Sections 3-7*** are intended to be used together to establish a long-term stability protocol. These sections combine, align, clarify and modernise content from ICH Q1A and ICH Q5C for primary stability studies. The sections provide:
  - Specific guidance for primary stability protocols
  - Guidance on minimum data recommendations at submission, attribute selection and identification of representative batches
  - Guidance on long-term and accelerated storage conditions
  - Clarity on where principles are applicable to other protocols, such as stability commitments or those to support post-approval changes.

Summary of Draft Guideline Content

Sections 8-11 provide guidance on stability studies intended to supplement the primary stability study.

- ***Section 8*** provides guidance on photostability that aligns with ICH Q1B and informs the recommended storage conditions for the drug product. The guidance in this section should be used in conjunction with the guidance in Section 2.
- ***Section 9*** provides stability recommendations for processing and holding times for intermediates. Content in this section is new guidance and articulates when data should be included in a regulatory submission and when it may be managed within the PQS.

Summary of Draft Guideline Content

Sections 8-11 provide guidance on stability studies intended to supplement the primary stability study.

- ***Section 10*** is new content and provides guidance on studies to support short-term storage conditions (which differ from in-use conditions) for products that include this on the label. This section is not applicable to all drug products.
- ***Section 11*** is new content and provides guidance on studies to support the in-use period and storage conditions for drug products.

Summary of Draft Guideline Content

- ***Section 12*** is new content and provides guidance on how to use the other sections of the ICH Q1 Draft Guideline with respect to reference materials, novel excipients and adjuvants.
- ***Section 13*** provides guidance on data evaluation, including:
  - General considerations for assigning re-test period and shelf life
  - Statistical evaluation, extrapolation and presentation of data
  - Content is aligned with current ICH Q1E and should be used in conjunction with Annex 2 when statistical approaches are applied.

Summary of Draft Guideline Content

- ***Section 14*** provides guidance on labelling and storage statements and excursions outside of the labelling claim derived from stability studies described throughout the guideline.
- ***Section 15*** provides guidance on stability commitments for product lifecycle management, including new guidance for post-approval changes. Content on commitments is consistent with ICH Q1A. Content on the introduction of new dosage forms is consistent with ICH Q1C.
- ***Sections 16 & 17*** are the glossary and references

Summary of Draft Guideline Content

Section 18 includes 3 Annexes:

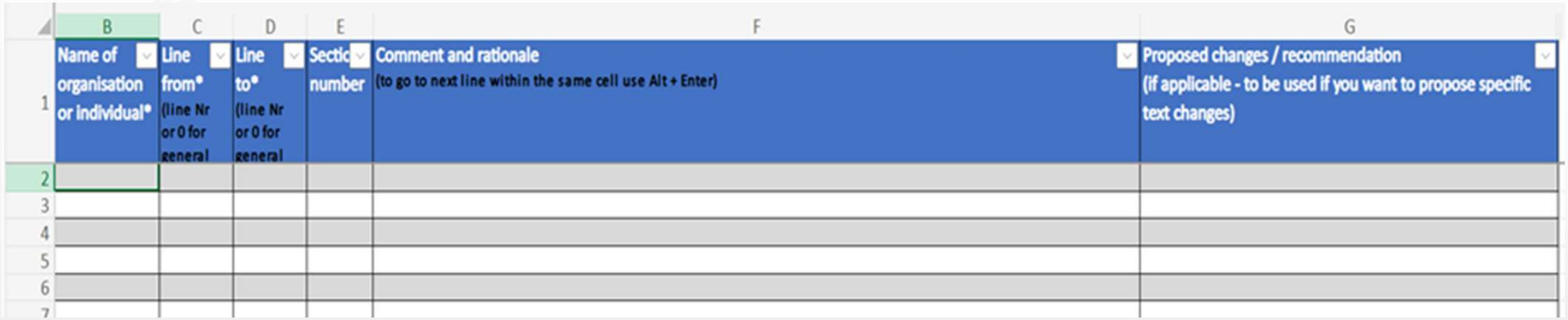
- ***Annex 1*** includes guidance on bracketing and matrixing currently captured in ICH Q1D. New guidance is provided on knowledge and risk-based protocol reductions.
- ***Annex 2*** provides guidance on stability modelling. It includes guidance currently provided in ICH Q1E and new guidance on using enhanced stability modelling.
- ***Annex 3*** provides stability guidance on ATMPs (Advanced Therapy Medicinal Products) which are new to ICH. This annex is supplemental to the core ICH Q1 Draft Guideline and is not a stand-alone guideline for ATMPs.

Recommendations for Commenting

Please do not provide duplicate comments through multiple organizations.	Every comment requires resolution, and duplicate comments prolong the resolution process.
If a comment is considered critical, please indicate this within the comment (Column F) and provide a rationale.	Reserve the classification of ‘critical’ for items that cannot be addressed through training or simple text revisions.
Please include recommendations for training material where a concern is too specific for the guideline or where further explanation is needed.	Guideline recommendations address a wide range of product types and scenarios. Training may also address specific situations likely to be commonly encountered.

Commenting Process

- The reviewer should follow the commenting process either per the ICH site or the regional authority they are sending their comments through.
- Column B “Name of organisation or individual*”: this is set up as free text and is mandatory
- Column C “Line from*”: this is set up to allow numbers only. If you want to submit a general comment, please enter 0 (zero). This field is mandatory
- Column D “Line to*”: If your comment applies to a single line, repeat the number of column C. This field is mandatory.



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1	Name of organisation or individual*	Line from* (line Nr or 0 for general	Line to* (line Nr or 0 for general	Sectio number	Comment and rationale (to go to next line within the same cell use Alt + Enter)	Proposed changes / recommendation (if applicable - to be used if you want to propose specific text changes)
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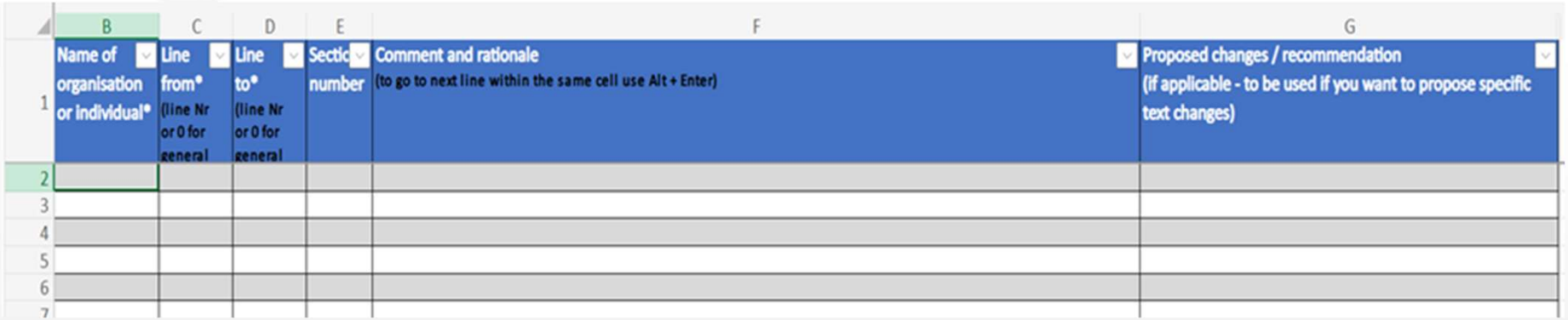
Commenting Process

- Column E “section number”: this is set up to allow numbers only. This is not mandatory but strongly encouraged.
- Column F “Comment and rationale”: It is not possible to fill in this column if columns B, C and/or D are not filled in. An error message will appear if B, C and/or D are empty. This column has been set up as wide as possible to allow long comments (up to 32,767 characters).
- Column G “Proposed changes/recommendation (if applicable)”: See column F.



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Useful links

ICH Q1/Q5C Concept Paper:
https://database.ich.org/sites/default/files/ICH_Q1Q5C_ConceptPaper_Final_2022_1114.pdf

ICH Q1/Q5C Business Plan:
https://database.ich.org/sites/default/files/ICH_Q1Q5C_BusinessPaper_Final_2022_1028.pdf

ICH Q1/Q5C Work Plan: ICH_Q1Q5C_EWG_WorkPlan_2024_0930.pdf

ICH Quality Discussion Group (QDG) Reflection Paper "Future Opportunities & Modernization of ICH Quality Guidelines: Implementation of the ICH Quality Vision from the ICH Quality Reflection Paper"
https://database.ich.org/sites/default/files/ICH_QDG_Recommendation_2021_1012.pdf

Contact

- **For any questions, please contact the ICH Secretariat:**

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