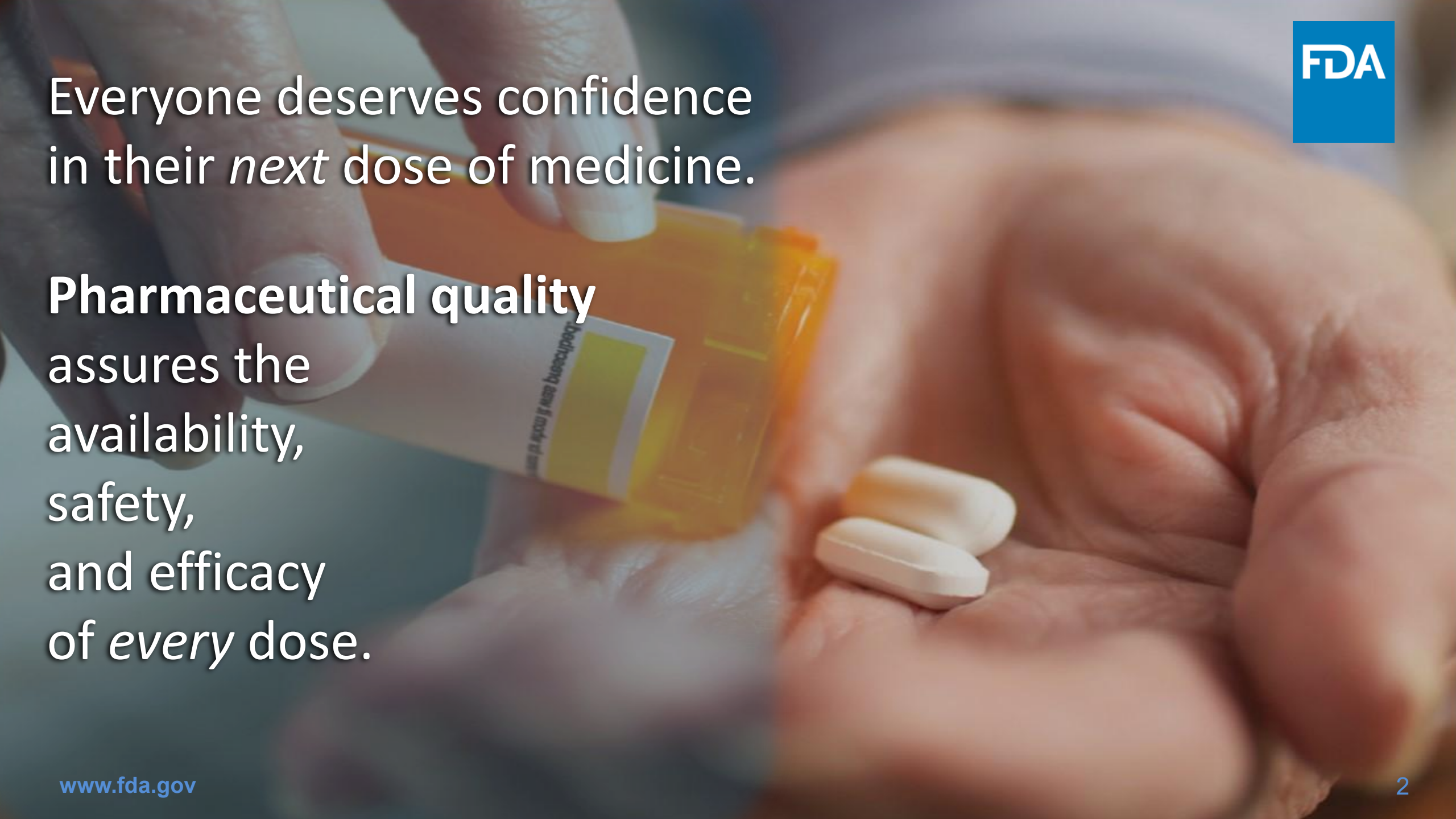
Advancing Stability Science for Biologicals:

Regulatory Perspectives on ongoing ICH Q1 Revisions and Predictive Stability Modeling

Ashutosh Rao, Ph.D.
Rapporteur, ICH Q1/Q5C Expert Working Group

Division Director, Office of Pharmaceutical Quality Assessment III
CDER/FDA

CASSS CE Pharm 2026



Everyone deserves confidence in their *next* dose of medicine.

Pharmaceutical quality assures the availability, safety, and efficacy of *every* dose.

Outline of presentation

- Updates on ongoing revisions to ICH Q1 for stability testing.

- Scientific and regulatory perspectives on updated topics for biological drug substance and products.
  - Points to consider for predictive stability modeling.

Disclaimer

- ***Although the ICH Q1 stability testing consensus technical document has been published for public commenting, it should be noted that the guideline is still in Draft status and is expected to change based on comments received during the ICH public consultation process.***
- ***The content of these slides and views expressed should not be construed as agreed or reflective of the final guideline.***

Why Revise the ICH Stability Guidelines?

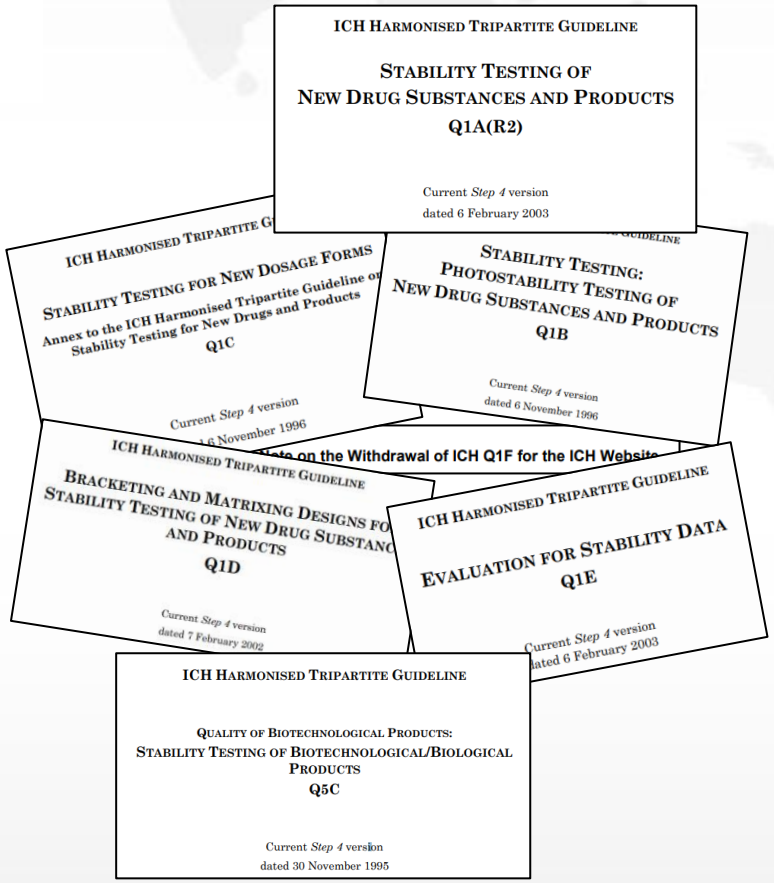
Final Concept Paper

Targeted Revisions of the ICH Stability Guideline Series (Guidelines ICH Q1A-F, ICH Q5C)

Endorsed by the Management Committee on 15 November 2022

Revision of the ICH Stability Guideline Series Q1A-Q1F and Q5C is 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.



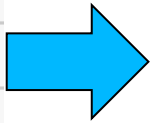
The envisioned result is a combined guideline, ICH Q1, with integrated annexes that address specific topics beyond the core principles on stability recommendations and to address product type specific recommendations, as required.

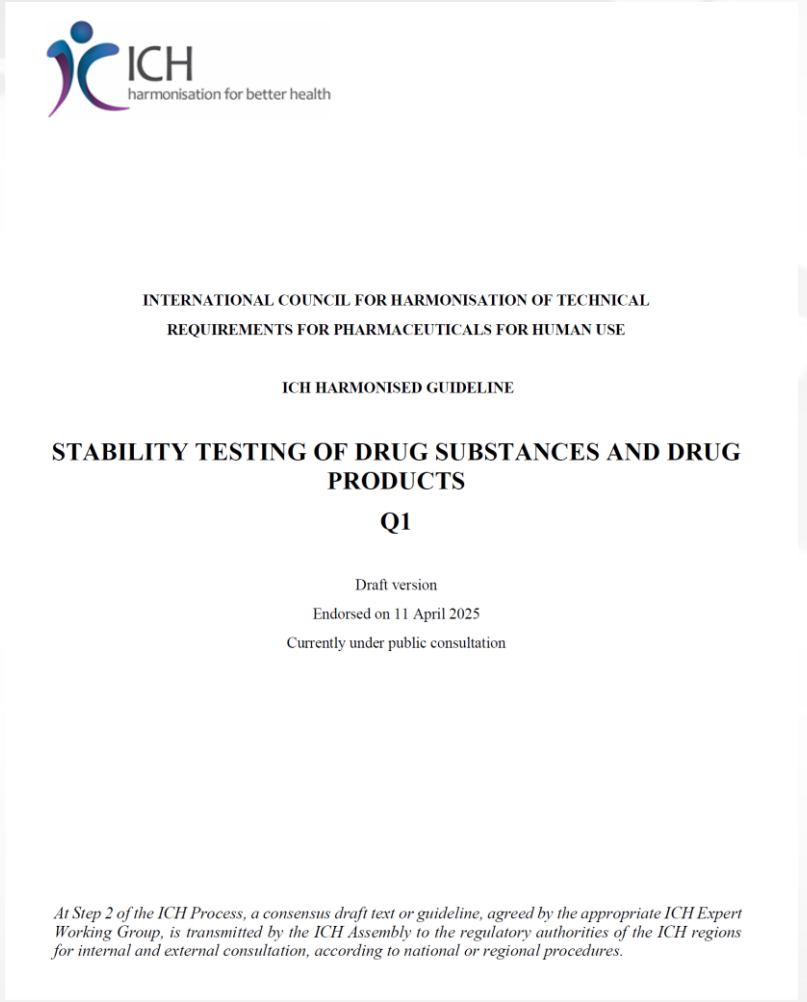
It is also recommended to update and supplement current training material.

Overview of changes with targeted revisions to Q1A-Q1F/Q5C

Q1A - Q1F Stability	
Q1A(R2)	Stability Testing of New Drug Substances and Products
Q1B	Stability Testing : Photostability Testing of New Drug Substances and Products
Q1C	Stability Testing for New Dosage Forms
Q1D	Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products
Q1E	Evaluation of Stability Data
Q1F	Stability Data Package for Registration Applications in Climatic Zones III and IV

Q5C	Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products





INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

STABILITY TESTING OF DRUG SUBSTANCES AND DRUG PRODUCTS

Q1

Draft version

Endorsed on 11 April 2025

Currently under public consultation

At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.

© 2023 DIA, Inc. All rights reserved.

ICH Step-wise Procedure

ICH harmonisation for better health

CONTACT REGISTER

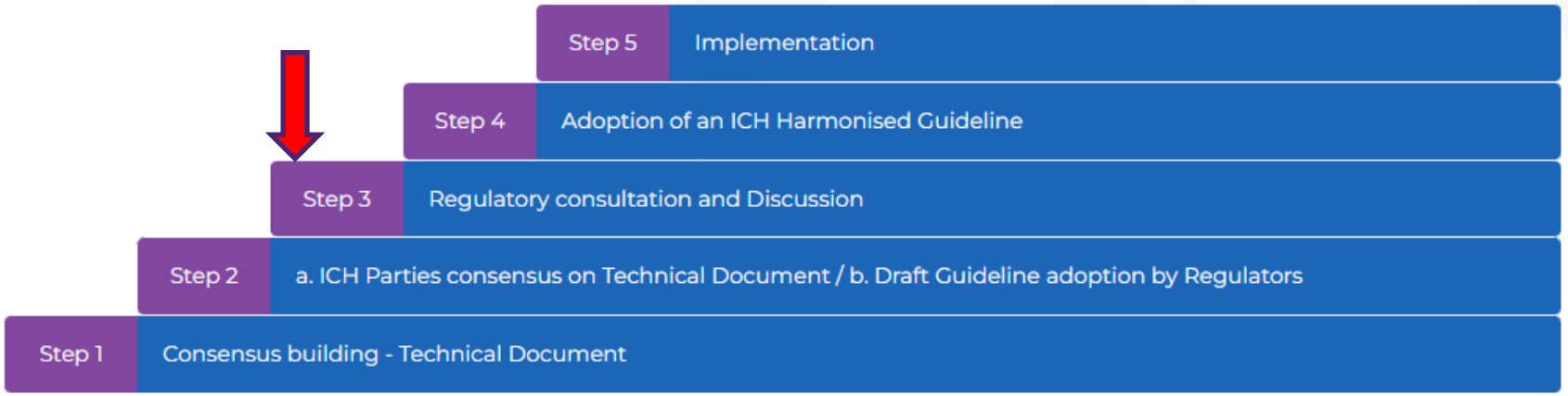
OSEM

HOME | ABOUT ICH | WORK PRODUCTS | MEETINGS | TRAINING | NEWSROOM | Search...

Home \

Formal ICH Procedure

The Formal ICH Procedure is a step-wise procedure consisting of 5 steps (see below, click to have information on a particular step). This procedure is followed for the harmonisation of all new ICH topics.



The procedure is initiated with the endorsement by the ICH Assembly of a Concept Paper and Business Plan. An Expert Working Group (EWG) is subsequently established.

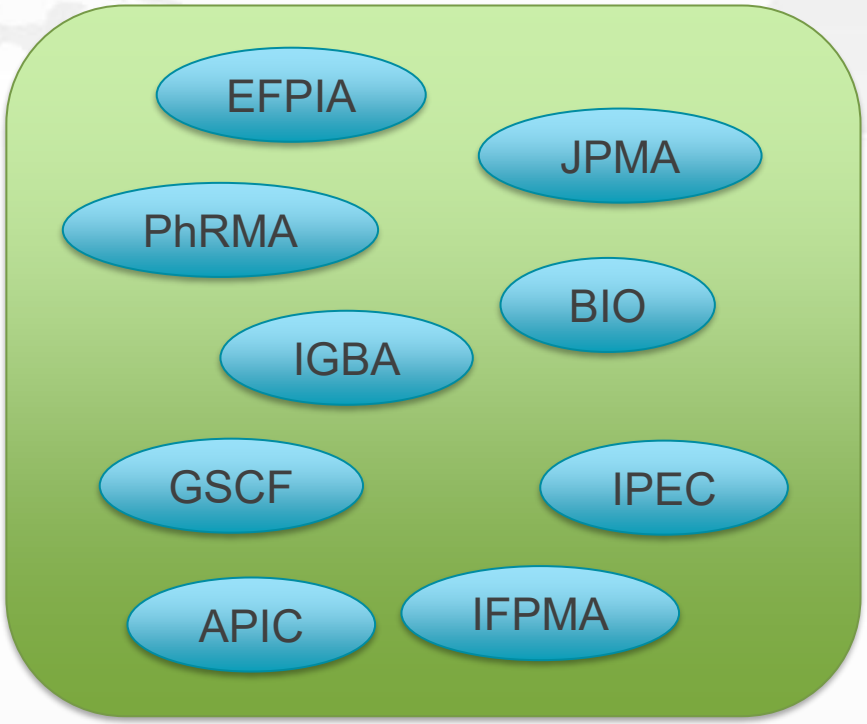
The EWG works to develop a draft Guideline and bring it through the various steps of the procedure which culminate in *Step 5* and the implementation in the ICH regions of a Harmonised Guideline.

Related Links

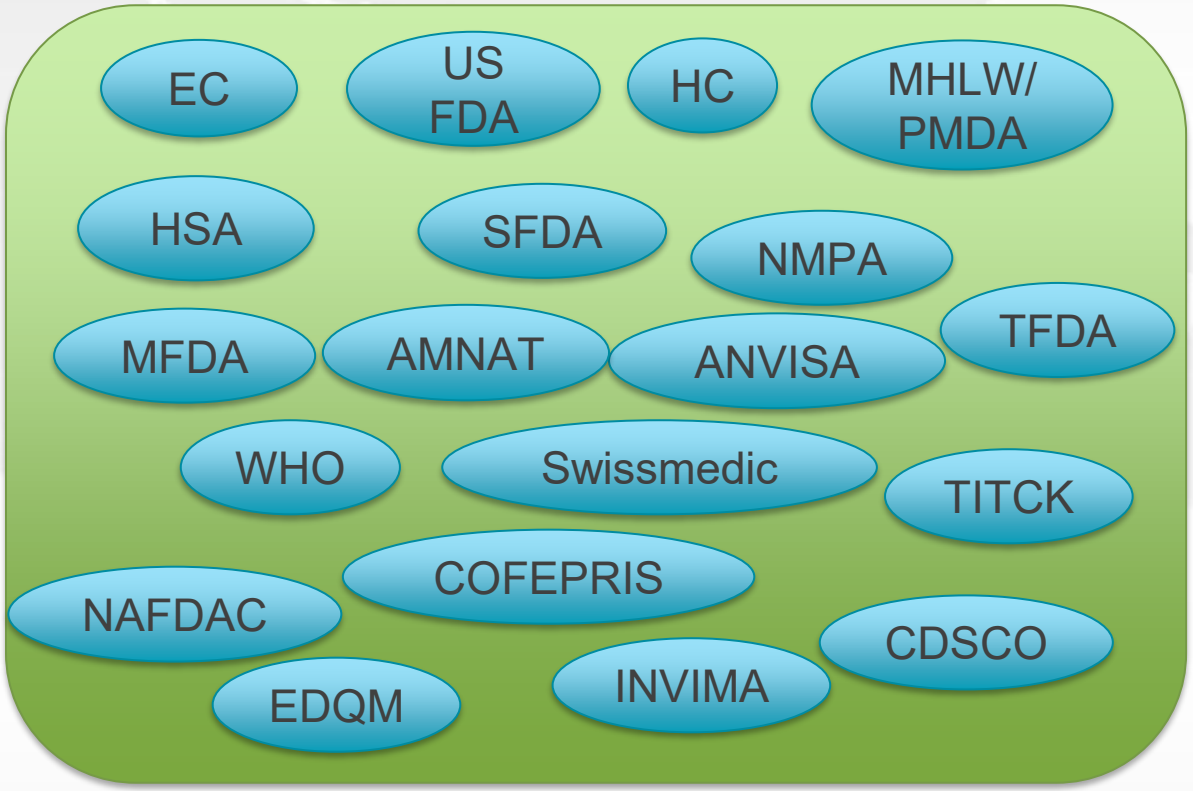
Open Consultation
ICH Guidelines

Representation in the ICH Q1/Q5C EWG

Industry



Regulators



Pre-Step 2 Rapporteur: PhRMA | Current Rapporteur: US FDA
Pre-Step 2 Regulatory Chair: US FDA | Current Regulatory Chair: ANVISA, Brazil

Current status

- As a part of Step 3, we completed regional regulatory consultation stage.
- The public commenting period was open between April 2025 and September 2025 across participating ICH regions and through the ICH Secretariat.
- Comment discussion and revisions are currently in progress by the ICH Q1/Q5C Expert Working Group.
- Finalization of Step 3 Experts Draft Guideline is expected by December 2026. Adoption (Step 4) and implementation (Step 5) of the ICH harmonized guideline will follow Step 3 finalization.
- Training materials are also being developed to support the finalized document.

© 2023 DIA, Inc. All rights reserved.

ICH Q1: Draft Guideline Content

1. Introduction
2. Development Stability Studies Under Stress and Forced Conditions
3. Protocol Design for Formal Stability Studies
4. Selection of Batches
5. Container Closure System
6. Testing Frequency
7. Storage Conditions
8. Photostability
9. Stability Considerations for Processing and Holding Times for Intermediates
10. Short-Term Storage Conditions
11. In-Use Stability
12. Reference Materials, Novel Excipients and Adjuvants
13. Data Evaluation
14. Labelling
15. Stability Considerations for Commitments and Product Lifecycle Management
16. Glossary
17. References
18. Annexes
    - Annex 1: Reduced Stability Protocol Design
    - Annex 2: Stability Modelling
    - Annex 3: Stability of Advanced Therapy Medicinal Products (ATMPs)

ICH Q1: Summary of Draft Guideline Content

1. Introduction
2. Development Stability Studies Under Stress and Forced Conditions
3. Protocol Design for Formal Stabi Studies
4. Selection of Batches
5. Container Closure System
6. Testing Frequency
7. Storage Conditions
8. Photostability
9. Stability Considerations for Processing and
10. Short-Term Storage Conditions
11. In-Use Stability
12. Reference Materials, Novel Excipients and Adju
13. Data Evaluation
14. Labelling
15. Stability Considerations for Commitments and Produ
16. Glossary
17. References
18. Annexes
    - Annex 1: Reduced Stability Protocol Design
    - Annex 2: Stability Modelling
    - Annex 3: Stability of Advanced Therapy Medicinal Products (ATMPs)

- ***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.

- ***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 Q5C.

ICH Q1: Summary of Draft Guideline Content

1. Introduction
2. Development Stability Studies Under Stress and Forced Conditions
3. Protocol Design for Formal Stability Studies
4. Selection of Batches
5. Container Closure System
6. Testing Frequency
7. Storage Conditions
8. Photostability
9. Stability Considerations for Processing and Hold
10. Short-Term Storage Conditions
11. In-Use Stability
12. Reference Materials, Novel Excipients and Adjuva
13. Data Evaluation
14. Labelling
15. Stability Considerations for Commitments and Produc
16. Glossary
17. References
18. Annexes
    - Annex 1: Reduced Stability Protocol Design
    - Annex 2: Stability Modelling
    - Annex 3: Stability of Advanced Therapy Medicinal Products (ATMPs)

Sections 3-7 are intended to be used together to establish a long-term stability protocol. These sections combine, align, clarify and modernize content from ICH Q1A and 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.

ICH Q1: Summary of Draft Guideline Content

1. Introduction
2. Development Stability Studies Under Stress and Force
3. Protocol Design for Formal Stability Studies
4. Selection of Batches
5. Container Closure System
6. Testing Frequency
7. Storage Conditions
8. Photostability
9. Stability Considerations for Processing and Ho
10. Short-Term Storage Conditions
11. In-Use Stability
12. Reference Materials, Novel Excipients and Ad
13. Data Evaluation
14. Labelling
15. Stability Considerations for Commitments and Pr
16. Glossary
17. References
18. Annexes
    - Annex 1: Reduced Stability Protocol Design
    - Annex 2: Stability Modelling
    - Annex 3: Stability of Advanced Therapy Medicinal Products (ATMPs)

Sections 8-11 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.
- Section 9 provides stability recommendations for processing and holding times for intermediates.
- 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 in-use period and storage conditions for drug products.

ICH Q1: Summary of Draft Guideline Content

1. Introduction
2. Development Stability Studies Under Stress and Forced
3. Protocol Design for Formal Stability Studies
4. Selection of Batches
5. Container Closure System
6. Testing Frequency
7. Storage Conditions
8. Photostability
9. Stability Considerations for Processing and Holding
10. Short-Term Storage Conditions
11. In-Use Stability
12. Reference Materials, Novel Excipients and Ad
13. Data Evaluation
14. Labelling
15. Stability Considerations for Commitments an
16. Glossary
17. References
18. Annexes
    - Annex 1: Reduced Stability Protocol Design
    - Annex 2: Stability Modelling
    - Annex 3: Stability of Advanced Therapy Medicinal Products (ATMPs)

- **Section 12** is new content and provides guidance on how to use the other sections of the guideline with respect to reference materials, novel excipients and adjuvants.
- **Section 13** provides guidance on data evaluation building on ICH Q1E
- **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.

ICH Q1: Summary of Draft Guideline Content

- **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) that is new to ICH. This annex is supplemental to the core guideline and is not a stand-alone guideline for ATMPs.

18. Annexes
    - Annex 1: Reduced Stability Protocol Design
    - Annex 2: Stability Modelling
    - Annex 3: Stability of Advanced Therapy Medicinal Products (ATMPs)

Highlights of new or revised content in current Step 3 draft document

- Comprehensive principles covering synthetic chemical entities, biologics, and advanced therapy medicinal products with expanded scope and a preamble for the reader
- Risk-based approaches and applications of prior knowledge throughout the stability assessment process
- Considerations for drug components of DDCs and impact of novel excipients, adjuvants on stability
- Stability considerations for drug substance, drug product, intermediates, holding times, and introduction of short-term storage conditions
- Expanded guidance on in-use stability and lifecycle management for post-approval changes related to stability
- Enhanced data evaluation methods to determine re-test period or shelf life, including clarification on 'start of shelf life' and proposed re-testing protocols for frozen biologic drug substances
- Expanded concepts of reduced protocol design for more efficient stability testing strategies
- Modernized guidance on extrapolation and enhanced stability modeling, including statistical considerations, model development/validation/verification strategies and supporting examples
- Comprehensive glossary with new or revised definitions to support understanding of updated concepts
- Integration of current scientific advances and regulatory best practices to provide a consolidated, modernized approach to stability testing

Useful links

FDA Draft Guidance: Q1 Stability Testing of Drug Substances and Drug Products
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q1-stability-testing-drug-substances-and-drug-products

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:
https://database.ich.org/sites/default/files/ICH_Q1_EWG_WorkPlan_2025_0725_FINAL.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

U.S. FOOD & DRUG ADMINISTRATION

Regulatory Perspectives on Predictive Stability Modeling

ICH Q1: Federal Register Publication

Title: Q1 Stability Testing of Drug Substances and Drug Products; International Council for Harmonisation; Draft Guidance for Industry; Availability

- **Docket No.: FDA-2025-D-1106**
- Publication Date: 06/24/2025
- Commenting period ended: **08/25/2025**

To view the document:

Federal Register :: Public Inspection: Guidance: Q1 Stability Testing of Drug Substances and Drug Products; International Council for Harmonisation

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2025–D–1106]

Q1 Stability Testing of Drug Substances and Drug Products; International Council for Harmonisation; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled ''Q1 Stability Testing of Drug Substances and Drug Products.'' The draft guidance was prepared under the auspices of the

Limited Experiences with Stability Models

Predictive stability models have so far been largely included as supporting information or under unique circumstances such as an EUA.

- Prediction of the initial shelf life
- Setting storage and use conditions
- Setting specifications for stability and/or release
- Justification for in-process control strategies
- Supporting comparability and lifecycle changes
- Shelf life extensions

Broad Categories of Information Relevant to Science- and Risk-based Assessment of Stability Models

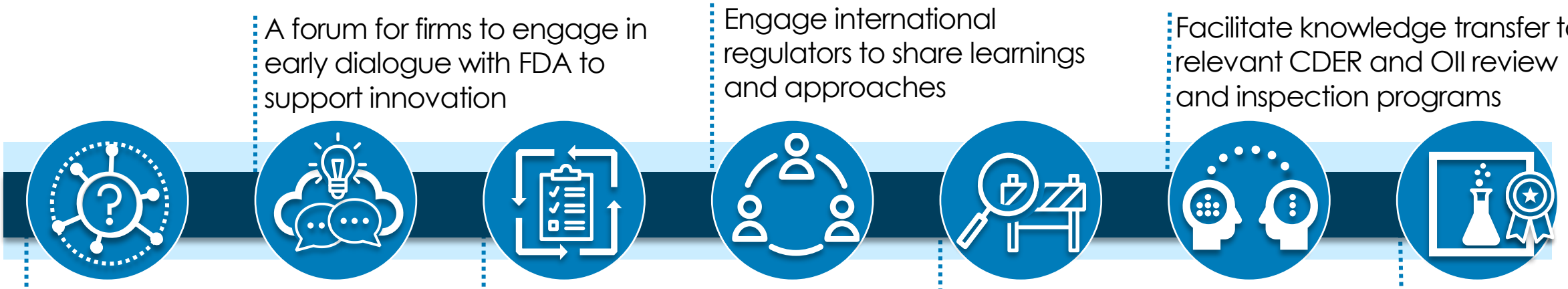
- **The Model** *(Context, Purpose, and Description)*
- **The Data** *(Input Data and Prior Knowledge)*
- **Modeling Tools** *(Statistical and Computational Tools)*
- **Model Suitability** *(Verification and Validation, Limitations)*
- **Lifecycle Management** *(Monitor, Adapt to Changes, Risk Management)*

Points to Consider when proposing Predictive Stability Models

- The Agency currently has limited experience with predictive stability models.
- While the ICH Q1/Q5C revisions are in progress and being actively discussed, we recommend aligning with current ICH recommendations and practices.
- Lessons learnt during COVID-19 and other expedited programs with stability strategies to assess degradation profile and support initial product shelf life could prove useful for additional products and development programs.
- Early engagement with Agency, either through a regulatory submission or other collaborations such as the Emerging Technology Program especially for very unique approaches such as AI, is encouraged to align on modelling approach and applicability for each context of use.

The Emerging Technology Program

Encourage and support the adoption of innovative technology to modernize pharmaceutical development and manufacturing through close collaboration with industry and other stakeholders



Serve as a centralized location for external inquiries on novel technologies

A forum for firms to engage in early dialogue with FDA to support innovation

Ensure consistency, continuity, and predictability in review and inspection

Engage international regulators to share learnings and approaches

Identify and evaluate potential roadblocks relating to existing guidance, policy, practice

Facilitate knowledge transfer to relevant CDER and OII review and inspection programs

Establish scientific standards and policy, as needed

The sponsor must justify how the proposed emerging technology meet two criteria:
(1) Pharmaceutical Novelty and (2) Product Quality Advancement

* For more information on how to apply to the ETP and develop a proposal:
https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/emerging-technology-program

Acknowledgements

- The ICH Q1/Q5C Expert Working Group
- Colleagues from the US FDA, Office of Pharmaceutical Quality
- Stakeholder feedback

Questions?