ICH Q1 Stability Guideline Revision
What's New?

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Background on Revision

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

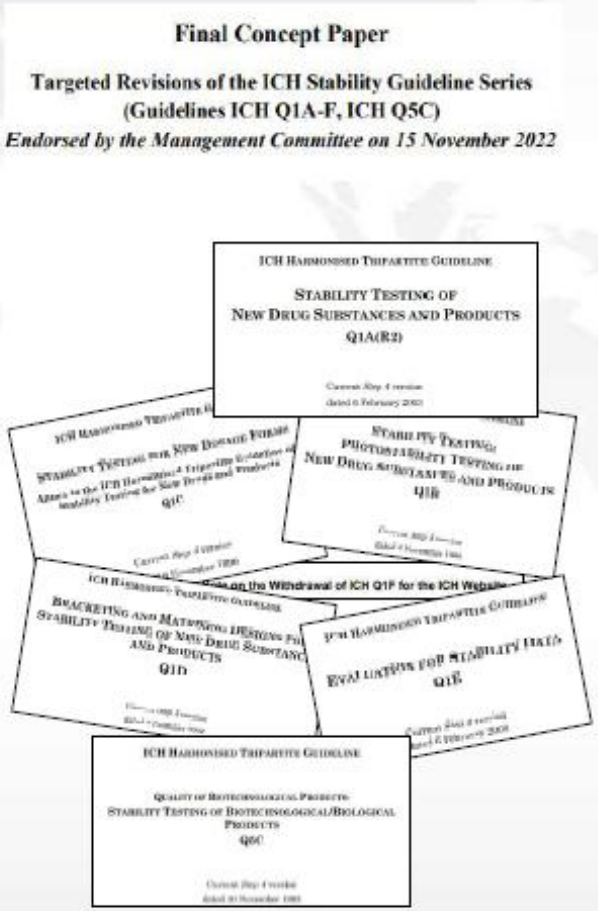
a) Streamline the series by combining the various guidelines into a single guideline focused on core stability principles;

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;

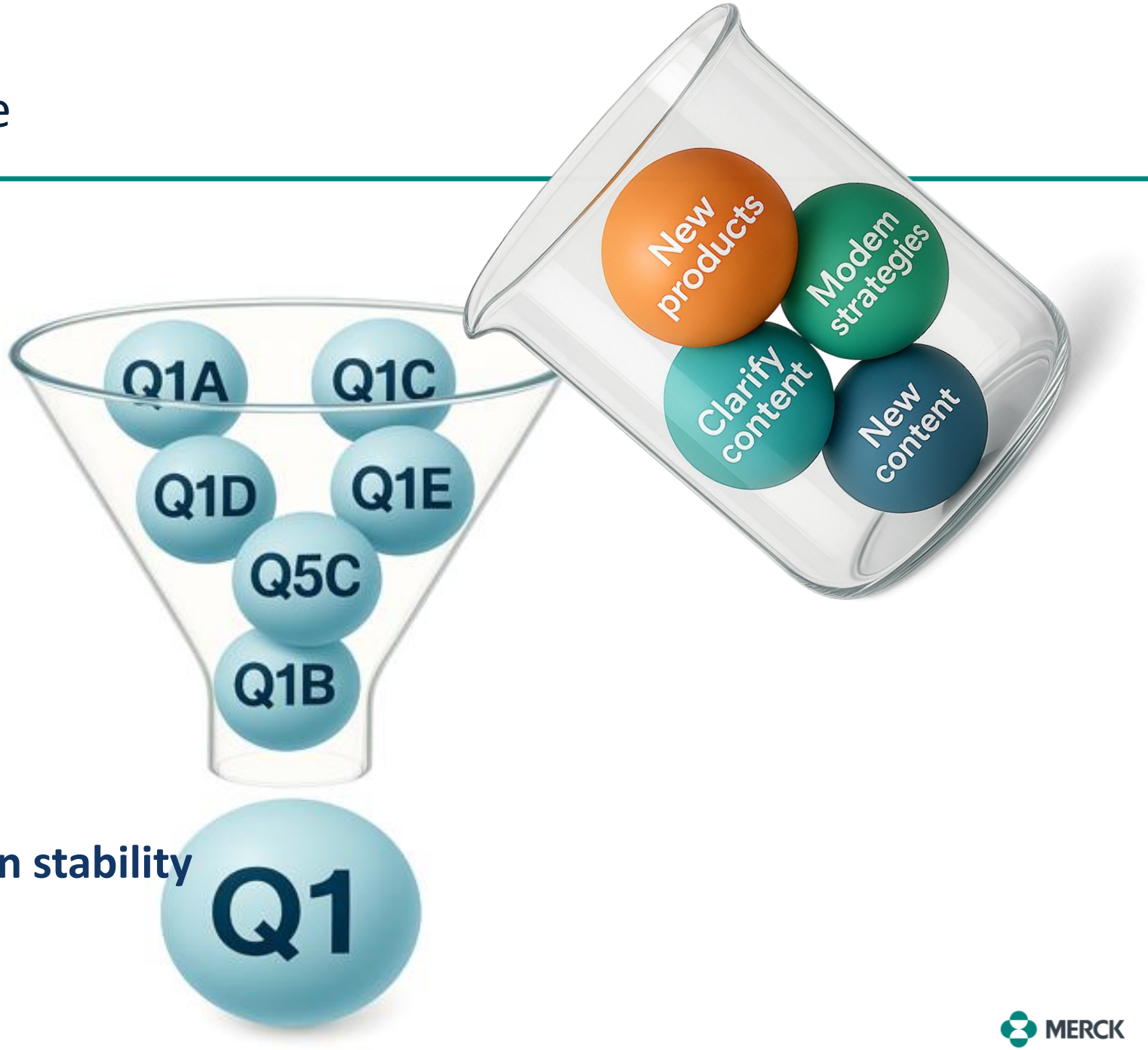
d) Consider inclusion of new topics, such as stability considerations for advanced therapies.

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.



Q1 Step 2 Presentation

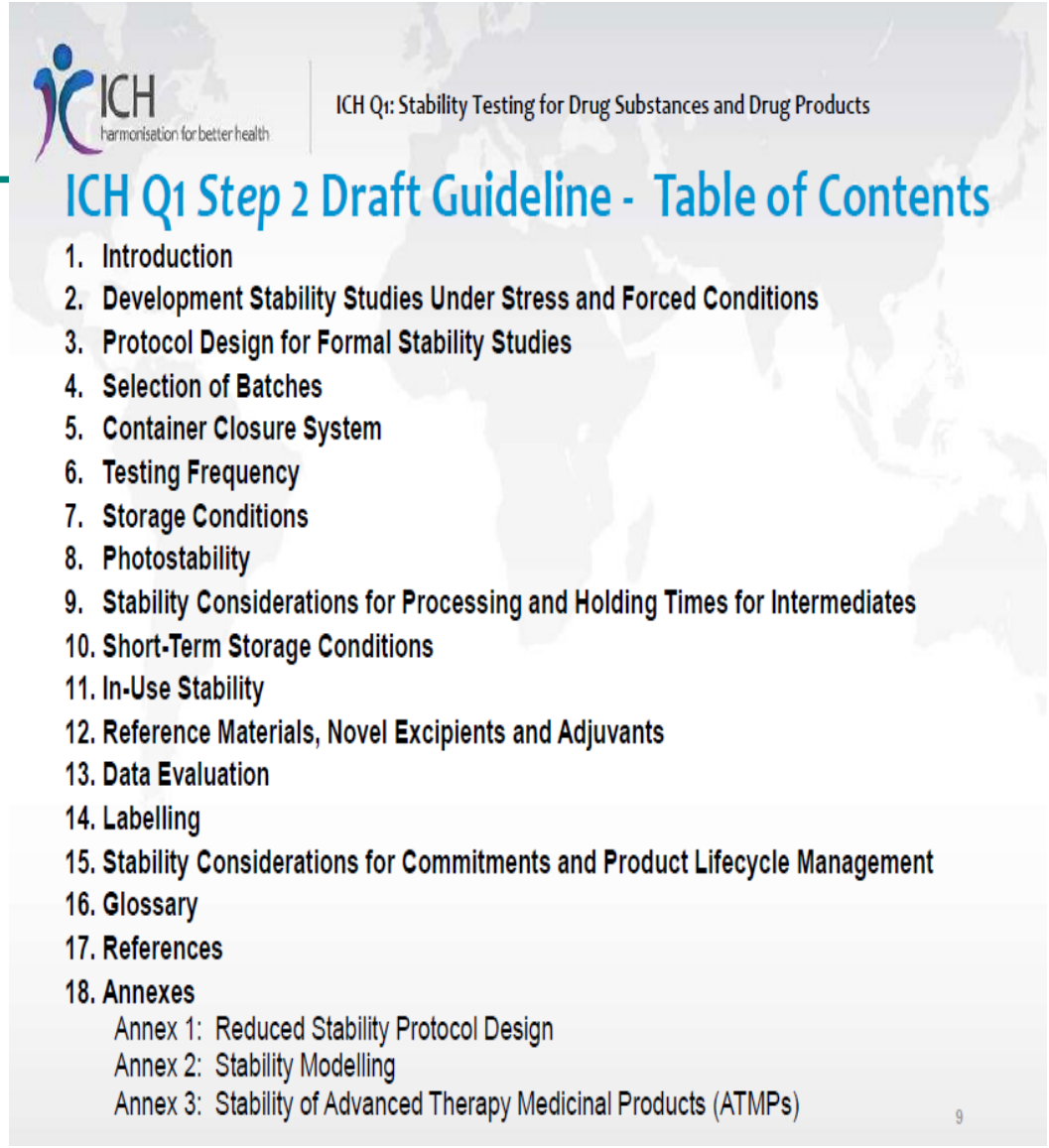
All-in-One Stability Guideline



Comprehensive, modern stability guideline

Enhancements in Q1 Revision

- Alignment on comprehensive scope of products
- Alignment on core principles for drug substance and drug product stability
- Sections to clarify expectations on current content in Q1 series and Q5C (photostability, data evaluation, storage conditions and testing frequency, etc.)
- Expanded guidance for various concepts, such as data evaluation, reduced protocol designs, stressed/forced degradation studies, glossary, etc.


ICH harmonisation for better health

ICH Q1: Stability Testing for Drug Substances and Drug Products

ICH Q1 Step 2 Draft Guideline - Table of Contents

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New Content

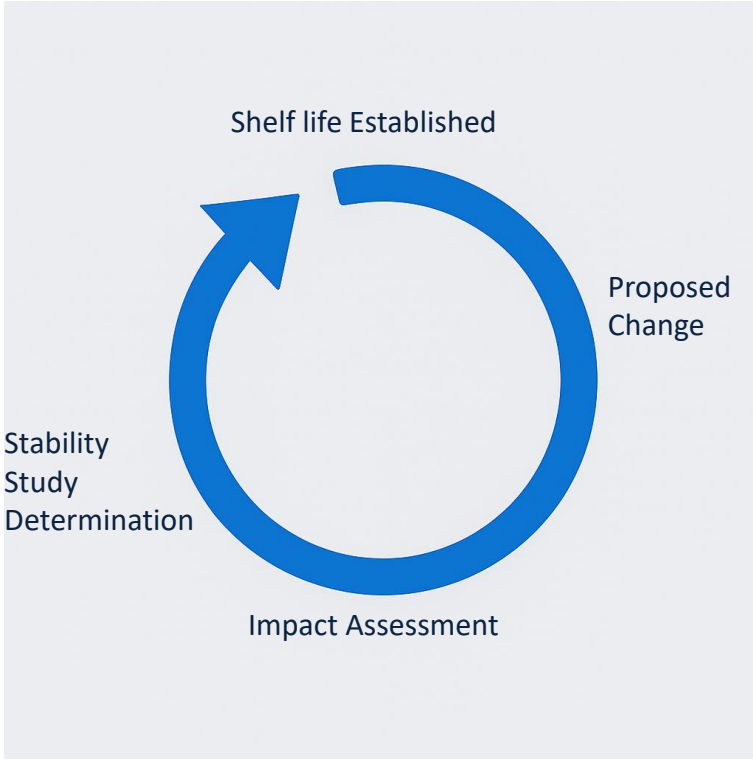
- Hold times for intermediates
- Short-term storage conditions (in label)
- In-use studies
- Clarify expectations for reference materials, novel excipients, and adjuvants
- Labeling and storage statements
- Stability commitments and expectations for post-approval changes (lifecycle)
- New Annex 2 for general principles and guidance on using enhanced stability modeling
- New Annex 3 for ATMPs

Short-term Storage Conditions vs In-Use Studies

Each appears on labeling, if implemented	Short-term storage- primary container closure is not breached and can be held for a prescribed duration as detailed on label	In-use storage- primary container closure is breached, prepared and stored prior to patient administration as detailed on label
• Instructions • Conditions • Duration	• Specific short-term storage condition stability study with considerations on number of batches, impact at end of DP shelf life, climactic zones, etc.	• In-use stability study with considerations on handling and preparation, extent of storage prior to use, multi-dose preparations, environmental factors, etc.

Stability Commitments for Lifecycle Management

- Clarification and Additional Details:
  - Commitment stability studies
  - Ongoing stability studies (annual)
- Product Lifecycle Stability Studies
  - Post-approval change scenarios to determine if new stability studies maybe needed
- Recommendations for stability studies for new dosage forms and strengths/concentrations



New Annex 2 Stability Modeling

- General principles and core study design elements for modelling
- Part 1: Statistical tools and models commonly used to assess stability data
  - Evaluation of variability between batches in single factor and multi-factor designs
  - Linear models to assess stability profile (mixed and fixed effects models)
- Part 2: Enhanced stability models for shelf life evaluation
  - General principles for model development, selection of data and parameters for model construct, evaluation of the model, risk management and life cycle considerations
- Model validation and verification

Considerations for Enhanced Stability Modelling

Statistical and Scientific Justifications

Well-characterized biological drug substances and drug products with a well understood stability profile

Model Validation- The process of determining the suitability of a model by challenging it with independent test data and comparing the results against predetermined performance criteria

Model Verification- The process of ensuring the model is implemented as intended. For example, confirmation that the modelled data for the initially proposed shelf life or re-test period are comparable to confirmatory experimental data

Shelf life setting based on more than just model output

New Annex 3 Stability of Advanced Therapy Medicinal Products (ATMPs)

- ATMPs- complex biological products, including somatic cell therapies, gene therapies, tissue-engineered products, etc.
- Additional information specific for ATMPs (used in conjunction with core)
- Study design considerations:
  - Short-term stability (days/months)
  - Patient-specific and/or small batch size
  - Unique temperatures (cryopreserved or warm)
  - Physical force effects
  - Product-specific stability attributes
  - Starting material impact

New For Biologicals

- Start of shelf-life definition
- Process hold times/Intermediates
- Primary stability batch criteria (representative of production)
- Well-Characterized Biologicals:
  - Retest period for frozen DS
  - Use of modeling to extend beyond real-time data
  - Extrapolation for biologic frozen drug substance

Why does this matter?

Harmonization of requirements across global health authorities

Clear guidance on a comprehensive approach to stability studies for global submissions

Enables science- and risk-based approaches to potentially shorten time to submission and time to market

Supports a wide range of product types and future therapeutics

Enables the use of new technologies and modern strategies for shelf life setting

Summary

- ICH Q1 Guideline revision combines ICH Q1A-E and Q5C to create a comprehensive stability guideline applicable to all types of marketed products
- Provides additional clarity and guidance on concepts already included in the current guidelines
- Provides new guidance on innovative, science- and risk-based approaches
- Includes new content on topics integral to a compressive stability program

Thank you