# THE CASE FOR REVISION TO THE ICH STABILITY GUIDELINES: AN INDUSTRY PERSPECTIVE

**CASSS-AT Europe**
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# REVISION OF ICH Q1 GUIDELINES ON STABILITY TESTING AND THE RELATED ICH Q5C GUIDELINE FOR BIOTECHNOLOGICAL PRODUCTS

ICH harmonisation for better health

**19 Members**
**36 Observers**

**Regulators with industry**

As of Dec 2021: Close to 70 ICH Guidelines:


- A proposal to update and modernised the Stability guidelines has been accepted by the ICH Management Committee and recommended to the Assembly *(ICH SOP section 2.3, Revision Procedure):*
- **June 2021**: The Assembly endorsed the proposal on *Stability Testing Guideline (ICH Q1)* –Targeted revisions and additional issues in the ICH Q1 series/Q5C, with an informal WG to be established with a delayed start ….. A Concept Paper outline will be provided for Assembly endorsement electronically in the June 2021 timeframe
- **November 2021**: *Targeted revisions and additional issues in the ICH Q1 series/Q5C*: start date in June 2022, when the ICH Secretariat will send the call to ICH Members and Observers for nominations of experts.

**24-25 May 2022: …..**

**The dates serve as links to ICH assembly meeting minutes**



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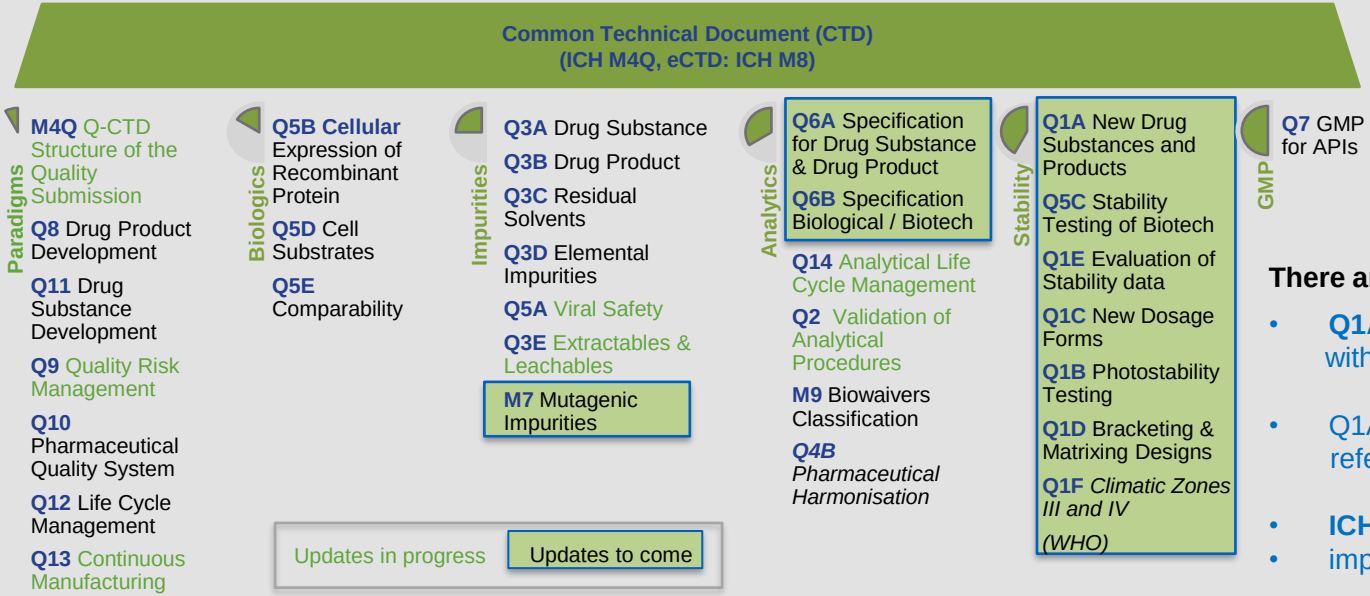
# PROPOSED MODERNISATION OF THE ICH QUALITY GUIDELINES




**There are 7 separate ICH Stability guidelines**

- **Q1A as a parent guideline,** from 1993 with 2 revisions and multiple supplements
- Q1A has elements for biologics and refers to **Q5C for "further guidance"**
- **ICH Q1 is a tier 1** guideline:
- implementation as a condition for ICH.



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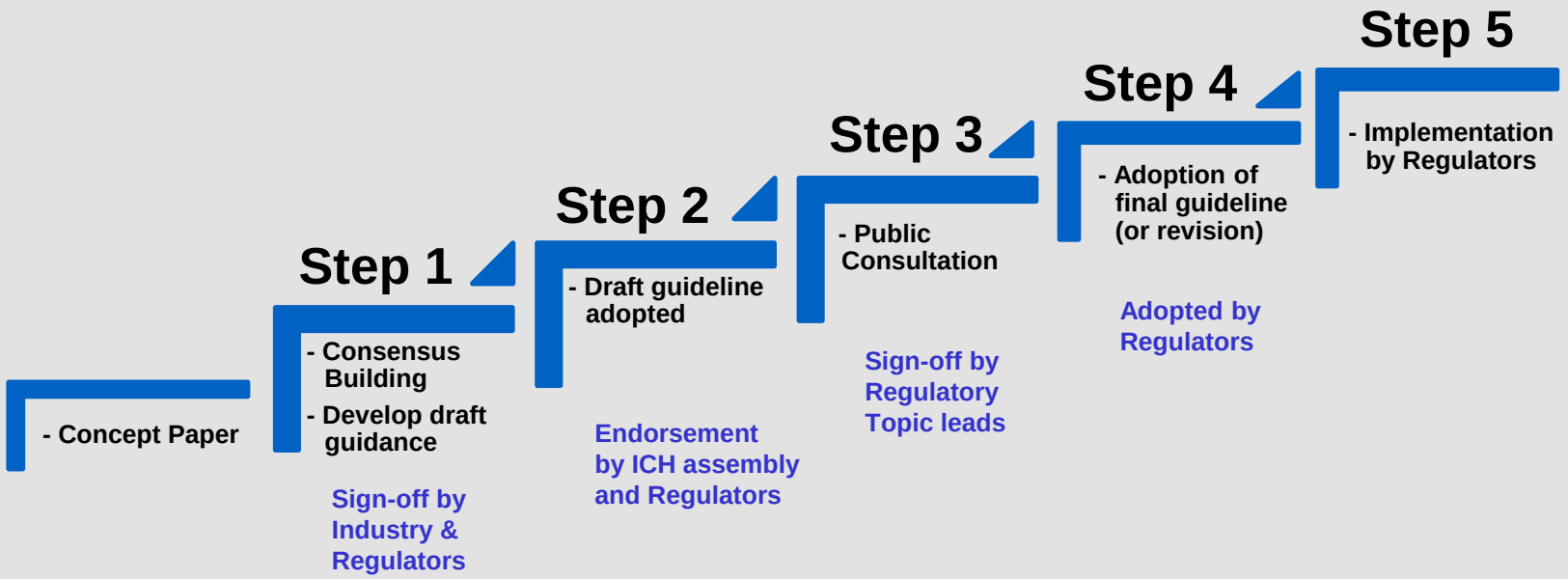
# FIVE STEP ICH PROCESS TO ACHIEVE A HARMONISED GUIDELINE

*(APPLIES TO NEW GUIDELINES AND REVISIONS)*




https://www.ich.org/page/formal-ich-procedure



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# ABOUT THE EFPIA STABILITY ICH SUPPORT TEAM

# PROBLEM STATEMENT

- **Update to align with more recent QbD and risk management ICH guidelines: Q8** (pharma dev), **Q9** (risk management), **Q10** (PQS) **and Q11** (DS development & manufacture)
- **Risk-based approaches to accelerate CMC are not described,** e.g. modelling, prior knowledge
- **Guidance considered as too prescriptive and interpretations too narrow** - e.g. batches, protocol
- **Confusion on elements of the Q1 series that apply to biologicals**
- **Guidance for newer therapeutic modalities is lacking**
- **Identified gaps in current guidance, include:**
  - In-use stability
  - Short-term end user stability
  - Integral drug-device combination (iDDC) products
  - Integrated, end-to-end stability



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# SOME PROPOSALS FROM INDUSTRY

# RESTRUCTURING OF ICH STABILITY GUIDELINES:
## *A PROPOSAL FROM INDUSTRY TRADE ASSOCIATIONS*

**Transfer most content from Q1A - E, Q5C, and potentially Q1F & WHO guideline into a single Q1 guideline with addenda / annexes**

- Experience in manufacturing biologicals, our scientific understanding of the products and analytical technology has increased vastly over the past 20 years
- **Guideline of stability concepts and principles** that emphasises the 'What' and 'When' rather than on the 'How' – *aligns to more recent guidelines*
- Remove ambiguity & uncertainty related to interpretation & application – *see Problem Statement*
- Harmonise between therapeutic modalities - small molecules, biologic, vaccines, oligonucleotides, cell-based therapies, gene therapy – *general principles and concepts for Stability testing & evaluation should apply to all.*
- **Annexes** for specific aspects relating to a particular modality **and Appendices** for examples – *see ICH Q8*

**There is now less need to distinguish between therapeutic Modalities**



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# PROPOSED SCOPE

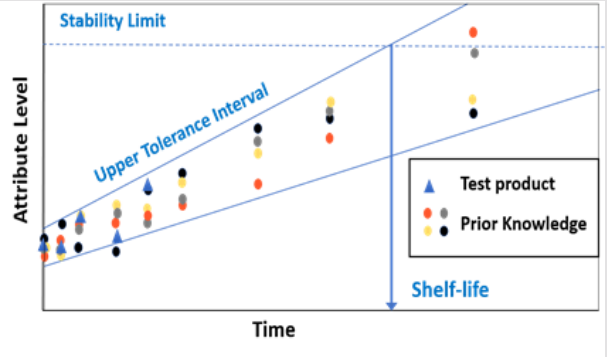
- **small, chemically synthesised** active pharmaceutical ingredient (API).
- well-characterised **proteins and polypeptides**, which are isolated from tissues, body fluids, cell cultures, or produced using rDNA technology,
- well-characterised proteins and polypeptides **conjugated** to a chemically synthesised moiety,
- well-characterised **cell-based** substances isolated from body tissues and may be modified,
- **viral vectors**, for example oncolytic viruses and vectors used for gene therapy and vaccines,
- **Integral drug-device combination** (iDDC) products and the medicinal product component of co-packaged drug-device products,
- and their associated drug products.

may apply to conventional vaccines, antibiotics, vitamins and newer pharmaceutical modalities.

# MODERNISATION (AND CMC ACCELERATION TOOLS) -1

## Enhanced product and process understanding (QbD):

- **Stability profile modelling tools:**
  - Kinetic modelling
    - ASAP
    - Arrhenius
    - Advanced kinetic analysis
  - Prior knowledge




- **Science & risk-based approach to:**
  - Number of batches – proportionate to risk, representative
  - Stability tests – focus on stability-indicating tests; shelf-life limiting
  - Testing frequency – lean/smart approach to testing

- **Greater use of prior knowledge**
  - Earlier representative development batches
  - Stability knowledge from 'like-molecules' (structure, stability profile etc)



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# MODERNISATION (AND CMC ACCELERATION TOOLS) - 2

- **An integrated (end-to-end), holistic, approach to stability from drug substance to finished drug product including end-user storage and handling**

- **Ensure guidance is suitable for anticipated developments in:**
  - **Digitalisation & automation**
  - **Analytical tools (e.g. multi-attribute methods)**
  - **Statistical analyses**
  - **CTD content changes (ongoing ICH M4Q revision)**

- **Harmonisation of expectations for lifecycle changes**

# SUMMARY OF BENEFITS TO STAKEHOLDERS

**Products to patients faster** with adequate assurance of stability and reduced ‘scrap’

**Supports innovation** and use of new stability testing tools including modelling

**Increased harmonisation of expectation and efficiency of** review

- Better structured dossiers, easier to review by agency
- Less jurisdiction-specific requirements
- Better understanding of agency/inspection expectations

**Consistent expectation and incorporation of modern science & risk-based approaches** that reduce redundancy and nonvalue-added stability testing



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# ACKNOWLEDGEMENTS


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