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ICH Efforts towards Developing a Unified ICH Q6(R1) and Modernizing Global Standards for Specifications Setting

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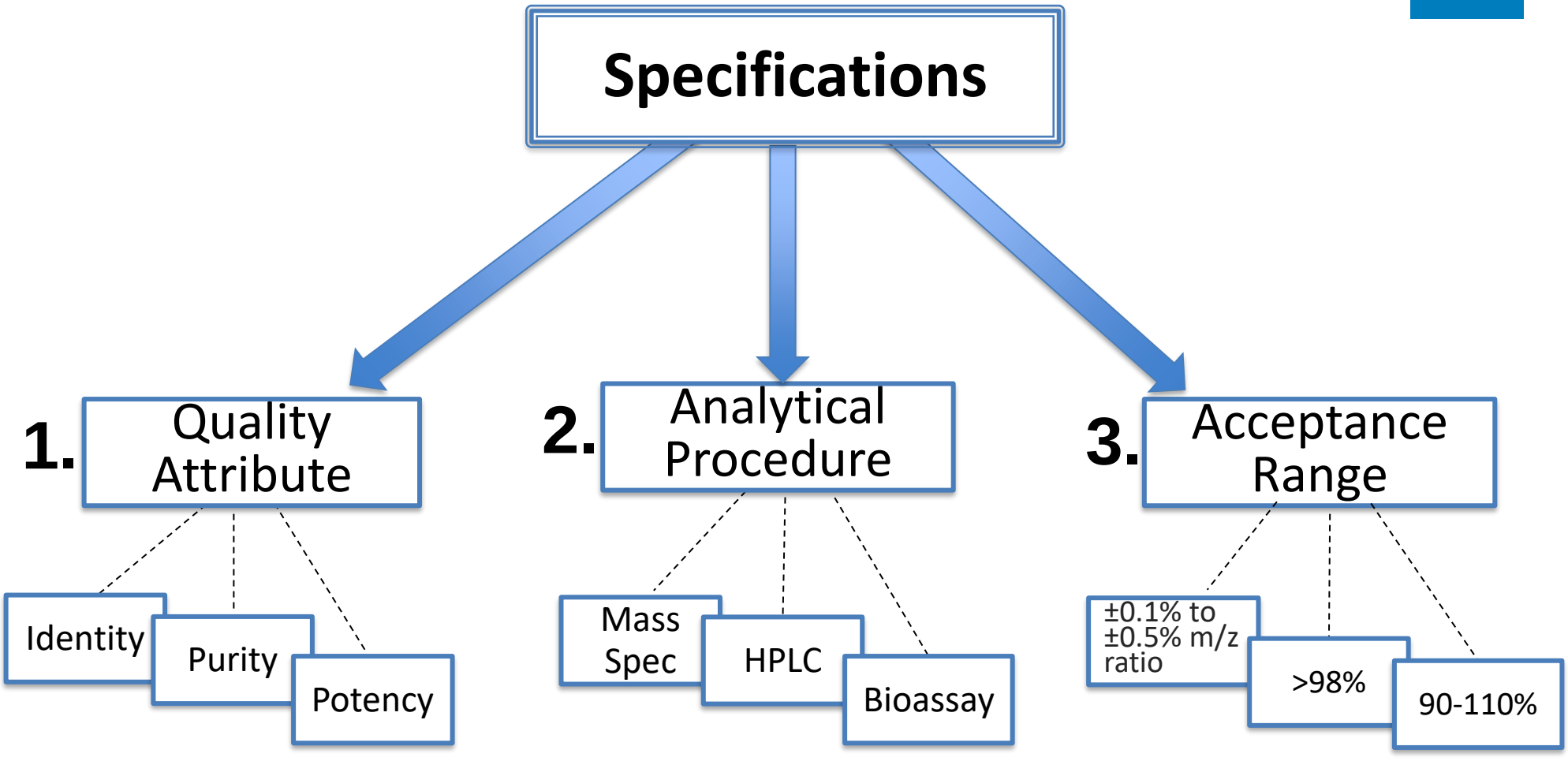
What are Specifications?



Outline

- Background
- Drivers
- Timelines
- Ways or working
- Early alignment
- Next steps

Quality Discussion Group (QDG) Evolution

2003 ICH Quality Vision

"Develop a harmonized pharmaceutical quality system applicable across the lifecycle of the product emphasizing an integrated approach to quality risk management and science"

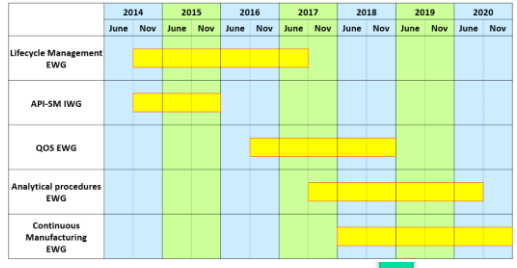
2005-14 ICH Quality Guidelines

- ICH Q8 Pharmaceutical Development (Parent guideline Nov 2005; Annex Nov 2009)[2]
- ICH Q9 Quality Risk Management (Nov 2005)[3]
- ICH Q10 Pharmaceutical Quality Systems (June 2008)[4]
- ICH Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Products) (May 2012)[5]
- ICH M7 mutagenic impurities

ICH Informal Quality Discussion Group (IQDG)

5 Year Plan for Quality Topics
Proposed to the Steering Committee
Minneapolis
June 3rd, 2014

2014 IQDG 5 year Plan



November 2018

ICH harmonisation for better health

Remit of the Informal Quality Discussion Group

22 October 2018

Endorsed by the ICH Management Committee on 13 November 2018

2019-2021

Quality Discussion Group Recommendation

18 August 2021

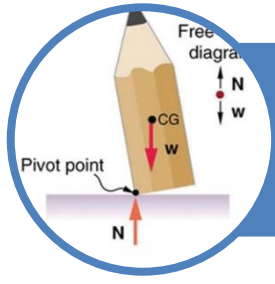
FUTURE OPPORTUNITIES & MODERNIZATION OF ICH QUALITY GUIDELINES: IMPLEMENTATION OF THE ICH QUALITY VISION[1] FROM THE ICH QUALITY REFLECTION PAPER[2]
ICH QUALITY DISCUSSION GROUP (2019-2021)

1. Topic Title
Stability Testing (ICH Q1, Q5C)
2. ICH Topic Description
Type of Harmonisation Actior
Category of Harmonized Proc
Brief statement of perceiv
History of the seven indepen
Multiple ICH guidelines in th i.e., Q1B, Q1C etc. These i guideline. This was done in t section where consensus wa

1. Topic Title
ICH Q6A and Q6B (dated September 8, 2020)
2. ICH Topic Description
Type of Harmonisation Action: New guideline ☐
Category of Harmonized Procedure: Quality ☒
Brief statement of perceived problem (caused
Both the ICH Q6A and Q6B Specifications guideli respectively, were harmonised in 1999 and their applicable and relevant over time without need for

Review existing ICH guidance and recommend updates

Is the guideline outdated due to new technologies / techniques?
The guideline is not up to date with current scientific understanding and principles?
Will an update address issues/alignment from other ICH guidance?
Will an update to the guideline address patient needs and accelerated access?
Will changes drive alignment e.g. replace regional-specific guidance, support implementation in new regions?



Stability (ICHQ1 series and Q5C)

Specifications (ICHQ6A and 6B)

Specifications (ICHQ6A and Q6B)

- From:
  - Two distinct guidances separating small and large molecules
  - Specification controls are the key to product quality
  - Based on batch experience
  - Specifications must be fixed in development
  - Aligned with long development and approval pathways

- To:
  - Holistic principles addressing all products with considerations for specific product types
  - Specifications are part of a holistic control strategy
  - Based on science and risk-based approach, platform and prior knowledge, and continuous processes considerations
  - Specifications should be on par with knowledge gained over the lifecycle
  - Aligned with rapid development and innovation

Problem Statement

- ICH Q6A and Q6B are of great value as these guidelines are based on scientific principles and on understanding and controlling quality attributes impacting product performance in well considered ways.
- In the 20+ years since these core guidelines were published, significant changes have occurred, and it is now vital that the guidelines are contemporized to address gaps and misalignment.

Drivers for the revision

- New therapeutic modalities (e.g., ATMPs, oligonucleotides, etc.)
- New manufacturing process technologies (e.g., continuous mfg.) and analytical capabilities (e.g., RTRT)
- Adoption of new ICH topics and/or significant updates to existing guidelines (Q2/Q14, Q1/Q5C, Q8-Q13)
- Introduction of Quality by Design, Control Strategy and risk/science-based concepts (Q8-Q11)
- Incorporating prior knowledge
- Increased need for expedited product development to address unmet medical needs

Anticipated Benefits

Patient Access

- Enable access to high-quality, safe and effective medicines to patients world-wide

Global Specification Standards

- Enable globally harmonized approach to setting specs using science- and risk-based principles and ensuring robust testing strategies to assure product quality

More efficient product development

- Facilitate global development with globally harmonized approach to setting specs clarifying regulatory expectations

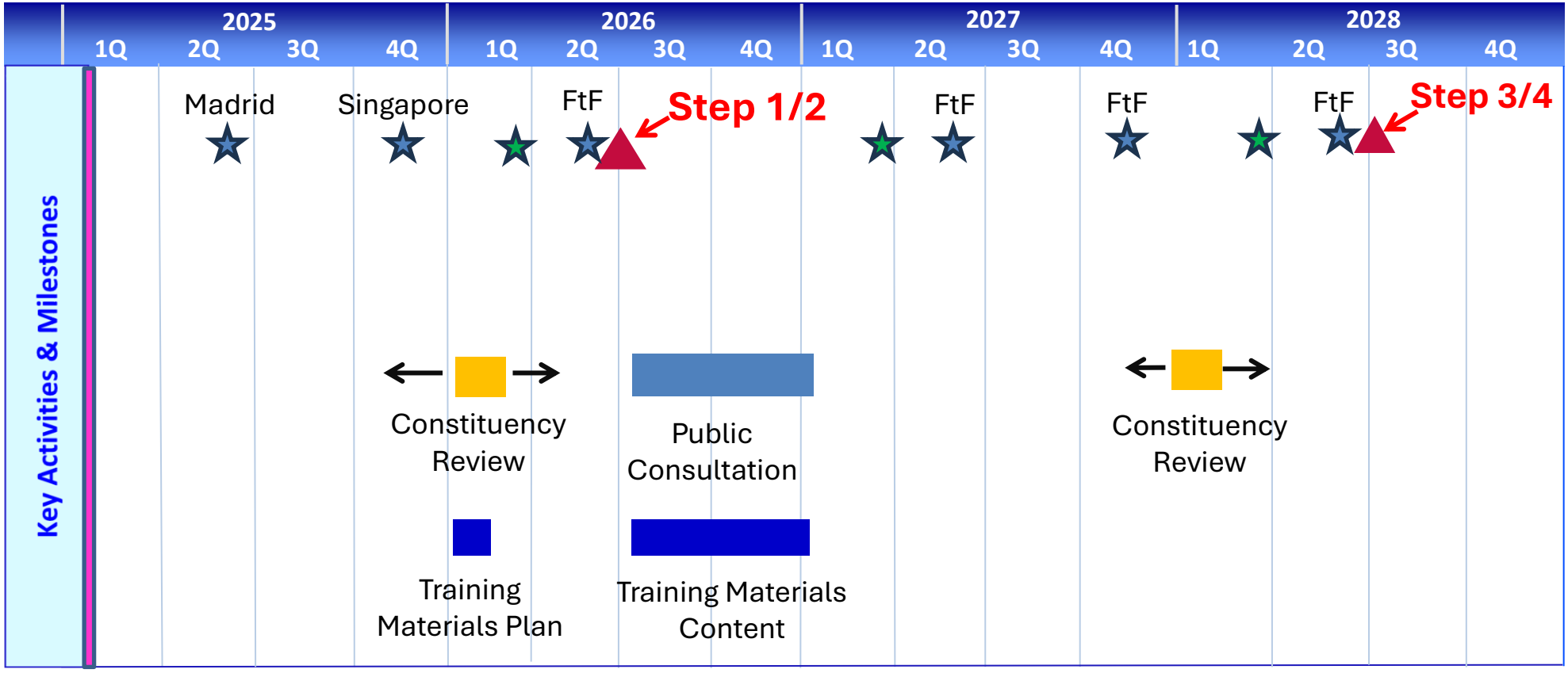
More efficient & consistent assessment

- Improve efficiency and consistency in regulatory assessment and decision-making.

Enhanced communication

- Enhanced communication between industry and regulators by bringing everyone on the same page.

ICH Q6(R1) Timelines



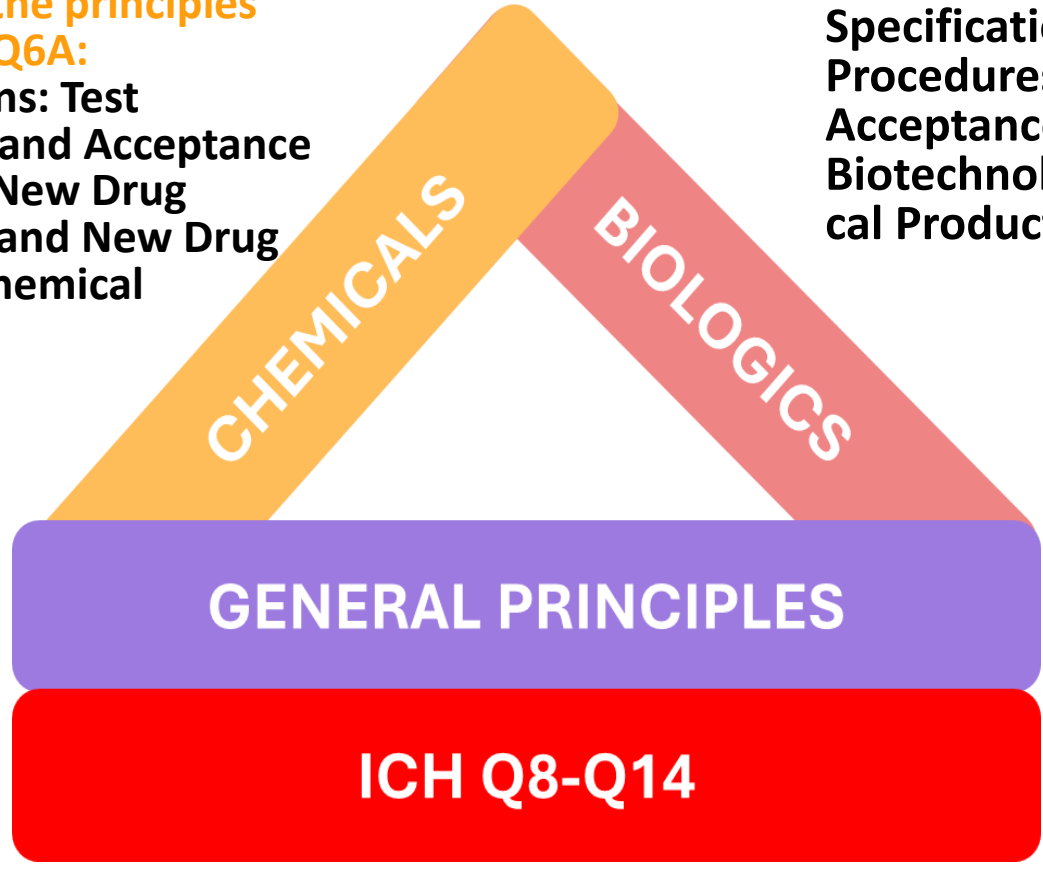
Concept paper endorsed by the MC in July 2024

Q6 Concept Paper link

Q6(R1) Strategy

Leveraging the principles outlined in Q6A:
Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances

Leveraging the principles outlined in Q6B:
Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products.



Identifying common unifying principles applicable to all product types

Considerable expansion of scope adding new biological modalities

Q6(R1) Guideline Structure

1. INTRODUCTION
2. GENERAL PRINCIPLES
3. CONSIDERATIONS FOR CHEMICALS
4. CONSIDERATIONS FOR BIOLOGICALS
5. GLOSSARY
6. REFERENCES
7. APPENDIXES (if needed)

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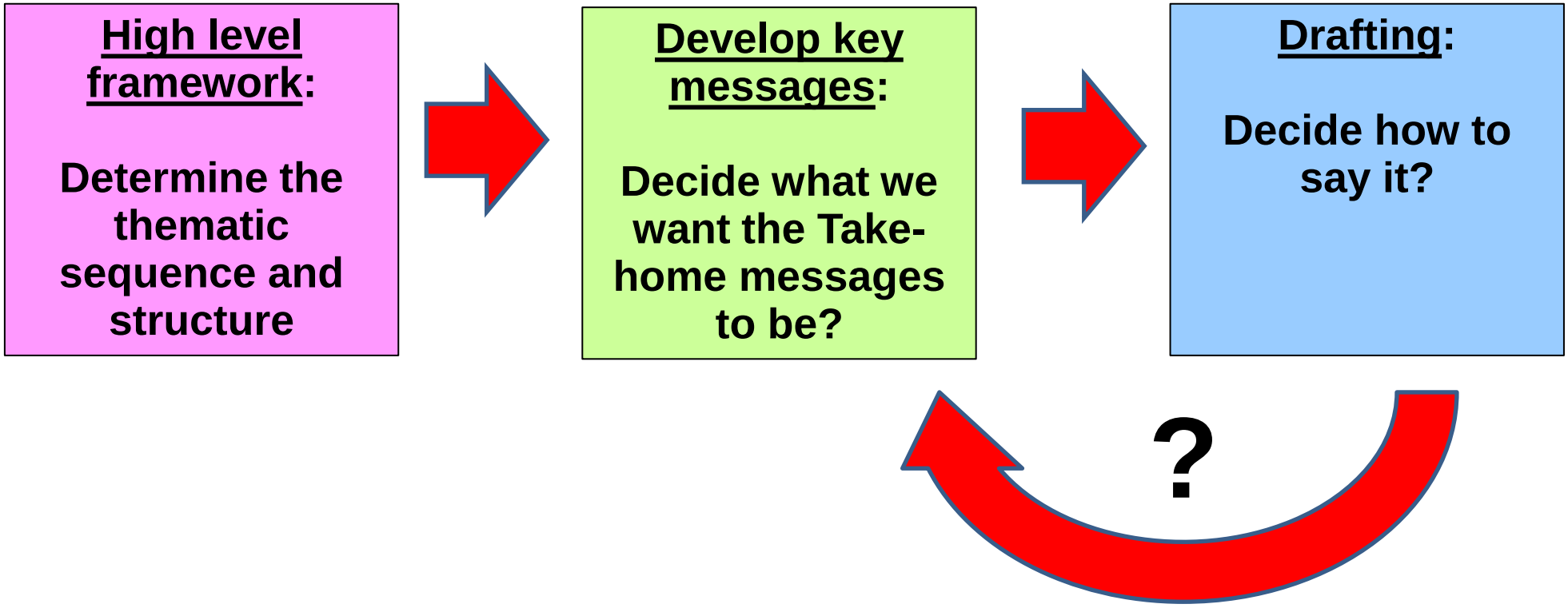
8. ANNEXES (if needed)

Approach to Drafting: Identify the Key Message(s) for each Section of the Outline as first step

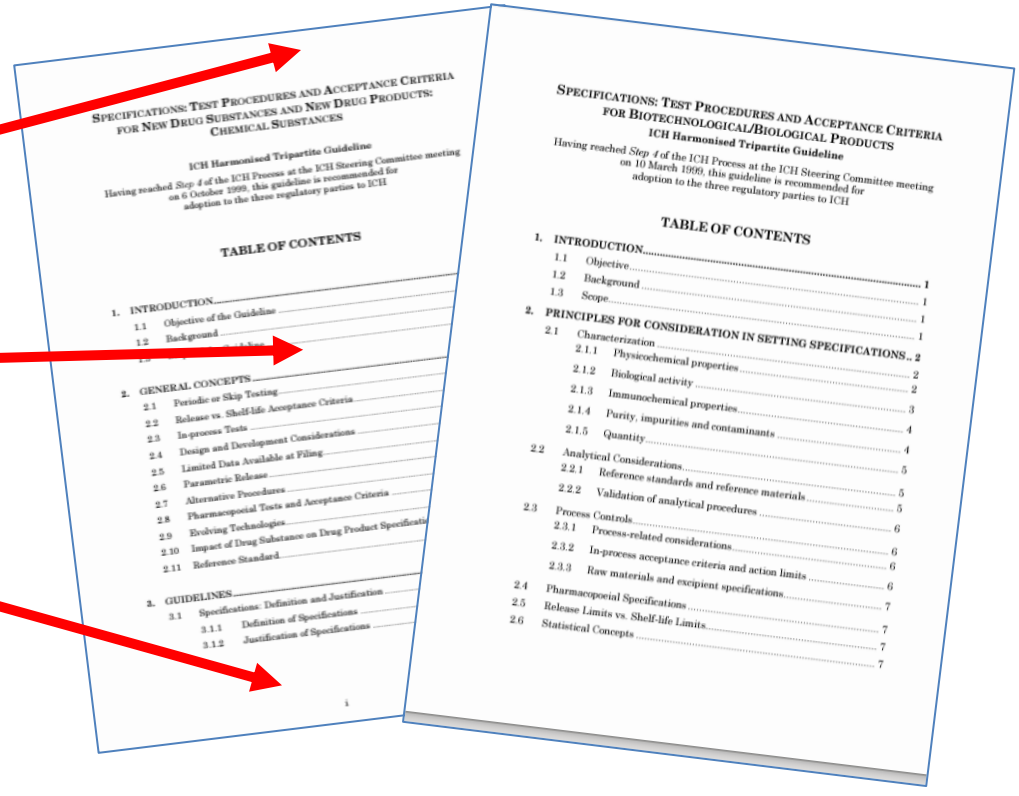


Tools to Assist with Drafting

QDG Gap Analysis

ICH QDG's Recommendations	Problems/Gaps Affecting Q6A & Q6B	Additional F
1. Clarify ICH Quality Guideline Linkages:		
i) Link applicable guiding principles from Q6A to Q6B. This includes clarifying the applicability of existing and to-be-updated content in Q6A to products within the Q6B scope. The QDG recommends including either: cross-references to the applicable Q6A sections/ text and/or adding Points to Consider (PTCs) in appropriate sections of Q6B.	Many of the key concepts and terminologies that need updating and aligning to other guidances are present in the introduction of Q6A and not repeated in Q6B (EPFIA). This link is currently missing.	
ii) Include an explanatory note in Q6A and Q6B that guiding principles from other ICH guidelines (e.g., Q2, Q3C, Q3D and M7, Q8, Q9, Q10, Q12, Q13 and Q14) are applicable in the	• Q6A and Q6B work together and in conjunction with other ICH guidelines as always (EPFIA). This link is currently missing; • Q6A and Q6B are 20 years old, and the contents are not up to date with	

Q6A and Q6B



Considerations for revision (1)

- ✓ Discuss how core principles apply to all product modalities, dosage forms and new technologies
- ✓ Align on the key principles of specifications setting as part of a control strategy (ICHQ8-14)
- ✓ Emphasize science and risk-based approaches
- ✓ Complement traditional reliance on batch data by emphasizing prior knowledge, science- and risk-based approaches
- ✓ Lifecycle management for the specification maintenance and update

Considerations for revision (2)

- ✓ Appropriate use of prior knowledge
- ✓ Clarify the role of pharmacopoeias in setting specs
- ✓ Shelf-life versus release specifications
- ✓ Link to and update in line with other ICH guidelines (e.g., Q2, Q3C, Q3D and M7, Q8-Q14)
- ✓ Address specific topics (e.g. analytical procedures and acceptance criteria for dissolution, biological reference standards, etc.)

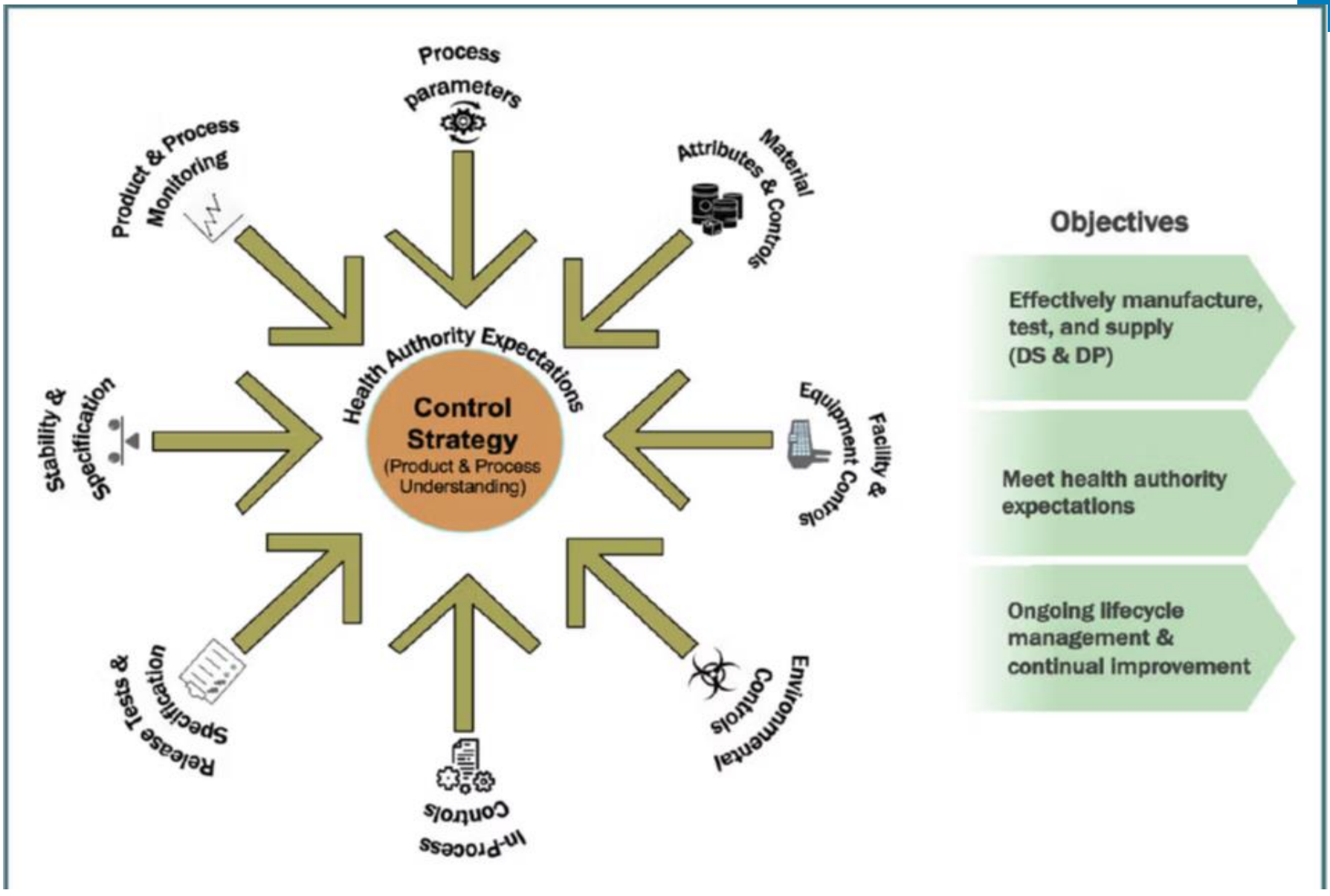
Guiding Principles

Assurance of quality as a function of knowledge

Knowledge can be gained through:

- Development studies
- Robust process understanding
- Physico-chemical characterization
- Structure-function relatioship
- Prior knowledge and platform experience
- Nonclinical/clinical evidence
- Lifecycle experience

Specifications are part of the overall control strategy



E. Ramnarine, Pharmaceutical Technology Pharmaceutical Technology, October 2023, V. 47, Issue 10

Key Takeaways

Key Takeaways (1)

- **Key comments on the initial draft of General Principles section:**
  - EWG acknowledges that the application of science and risk-based principles and a continuum of process and product knowledge are essential elements for modernization of specification setting.
    - Examples illustrating these ideas were developed and discussed in Montreal
    - These concepts require further discussion and refinement by EWG

Key Takeaways(2):
Patient Centric Specifications

Is there a need to introduce new terminology for ICH Q6(R1)?

Consensus by EWG:

- Not to introduce new terminologies in ICH Q6(R1) unless absolutely necessary
- Support the use of science- and risk-based concept/tools developed in Q8-Q14

Rationale:

- New terminology could mislead readers and increase complexity. Both “traditional” and “enhanced” approaches are patient-centric and relevant to patients.
- Science- and risk-based approaches used in Q-guidelines, e.g.,Q8-14 already covered patient relevant concept

Q6 Engagement with other ICH Groups to align on shared expectations

1. **Quality Discussion Group (QDG):**
   - To discuss background, clarify certain points, align on shared expectations and identify points of contacts for future interactions
2. **Q4B/Pharmacopeial Discussion Group (PDG)**
   - To discuss Interchangeability of pharmacopeial monographs, Decision made to defer to PDG/Q4B which already has efforts underway to address this
3. **CGTDG:**
   - Initial contact with CGTDG and Q6 leadership after Fukuoka meeting
   - Montreal meeting - A formal in-person meeting with broader membership for alignment on expectations and ways of working together
4. **ICH Q1/Q5C:**
   - Initial contact with CGTDG and Q6 leadership after Fukuoka meeting
   - Montreal meeting - A formal in-person meeting with broader membership Meeting with Q1/Q5C members to align on expectations for shelf-life/stability specifications

Thank you!