ICH Q14: Analytical Method Development Q2(R2):Validation of Analytical Procedures

Muhammad Shahabuddin, Ph.D.
Lab Chief
Laboratory of Biochemistry, Virology and Immunochemistry
Division of Biological Standards and Quality Control
Office of Compliance and Biologics Quality
CBER, FDA

Learning Objectives

- Provide an update on the development of ICH Guidelines Q14 and Q2(R2)

- Describe main topics addressed in these documents

Acknowledgement

Some contents of the slides are reproduced from *Step2* EWG presentation to ICH

Why Q14?

- No ICH Guideline for analytical procedure development
- No guidance on data supporting analytical development outcomes
- Inefficient communication during review
- Applicant has no opportunity to present basis for post-approval changes within the assay design

Why Revision of Q2(R1)?

- Developed in 1995 based on only chromatographic techniques
- Since then, newer combination techniques are available
- Multivariate tools have been applied as Process Analytical Technology (PAT) tools.

Guidance is needed to address analysis using these techniques

Current Status of Q14 and Q2(R2)

- The draft Q14 and Q2(R2) documents have been signed off as *Step 2* documents on March 24, 2022
- Issued by the ICH Regulatory Members for public consultation
- Draft document is available on ICH Website
- The documents were developed based on a Concept Paper and a Business Plan created in November 2018
- Targeting finalization as *Step 4* in May 2023

Key Principles

- Together ICH Q14 and ICH Q2(R2) describe the development and validation activities recommended during the lifecycle of an analytical procedure
- ICH Q14 describes the scientific principles for development, change management and submission requirement of analytical procedures for the minimal and enhanced approach.
- ICH Q2(R2) provides guidance for establishing, submitting and maintaining evidence that an analytical procedure is fit for purpose

Content Highlights of Q14-- (1)

- Describes science and risk-based approaches for developing and maintaining analytical procedures fit for intended use, in line with the systematic approach suggested in ICH Q8 and using principles of ICH Q9.
- Specifies a minimal approach and elements of an enhanced approach for analytical procedure development.
- Introduces concept of Analytical Target Profile (ATP). A prospective summary of the performance characteristics describing the intended purpose and the anticipated performance criteria of an analytical measurement
- Evaluation of Robustness and Parameter Ranges

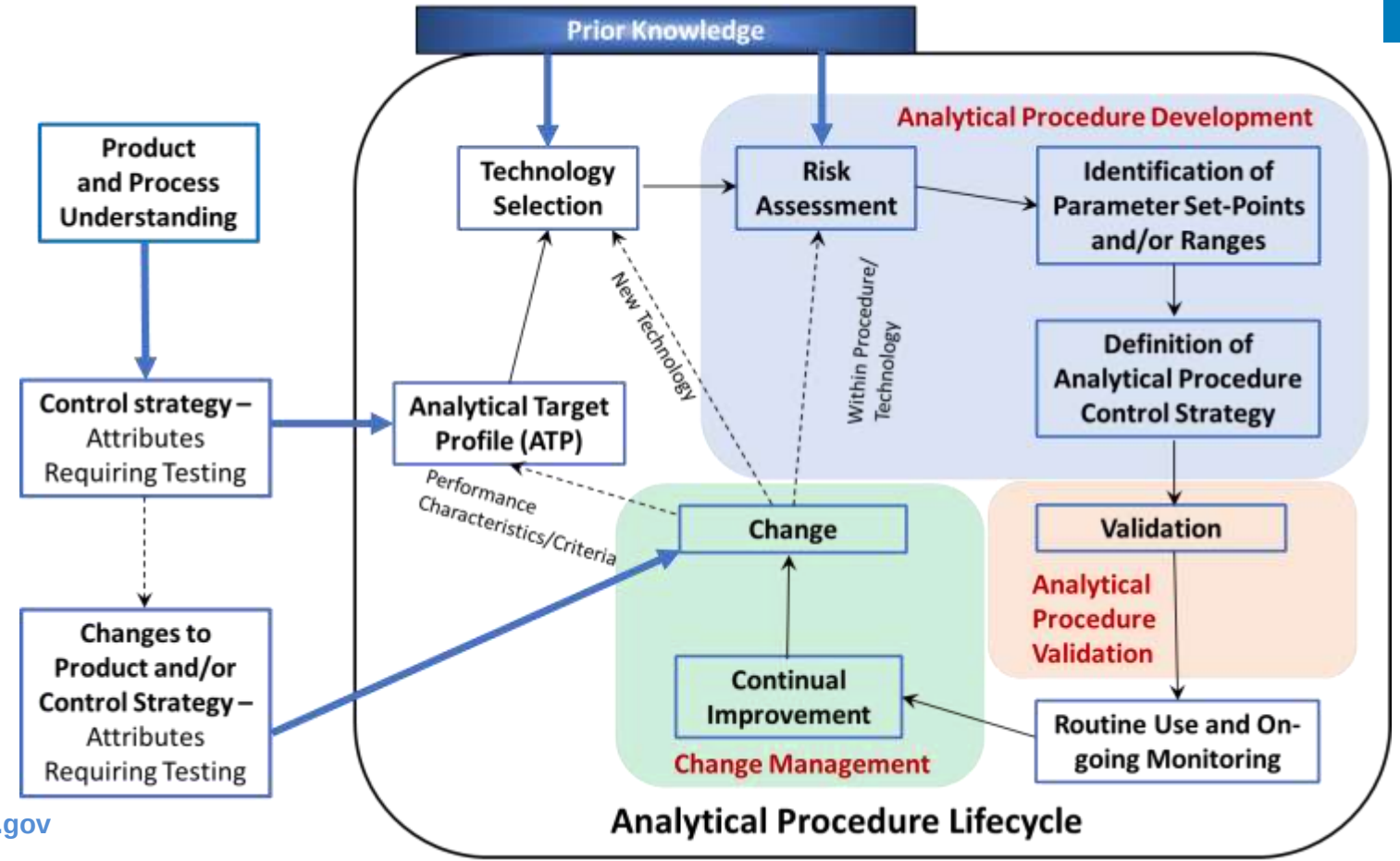
Content Highlights of Q14-- (2)

- Knowledge and Risk Management
- Analytical Procedure Control Strategy
- Established Conditions (ECs) for analytical procedure
- Lifecycle management and Post-approval Changes
- Describes considerations for the development of multivariate analytical procedures and for real time release testing (RTRT).

Content Highlights of Q14-- (3)

- Includes submission considerations of analytical procedure development and related lifecycle information in the Common Technical Document (CTD) format
- Annex A includes examples describing lifecycle management of analytical procedure

Concept of Analytical Procedure Lifecycle



Expected Benefits of Q14

- Harmonization of scientific approaches, key factors and terminology for analytical procedure development
- Increased understanding of analytical procedure
- Employing predefined performance characteristics guides development and facilitates regulatory change management of analytical procedures
- Enabling preventative measures and facilitating continual improvement by using more analytical procedure knowledge.
- Efficient Post-Approval Changes and Regulatory communication
- Guidance on demonstration of suitability for real time release testing

Objective of Q2(R2)

- Presents a discussion of elements for consideration during the validation of analytical procedures included as part of registration applications submitted within the ICH member regulatory authorities
- Guidance and recommendations on how to derive and evaluate the various validation tests for each analytical procedure
- Serves as a collection of terms, and their definitions
- Bridge the differences that often exist between various compendia and documents of the ICH member regulatory agencies
- Provides an indication of the data which should be presented in a regulatory submission

Content Highlights of Q2(R2) - (1)

- **Analytical procedure Validation Study**
- Design of an analytical validation study based on analytical procedure performance characteristics and technology selected
- Guidance on how prior knowledge can be incorporated into the validation study design
- Validation approaches during the analytical procedure lifecycle (partial, cross- and co-validation)
- Expected reportable ranges for common uses of analytical procedures
- Contains Table 1 : “Typical performance characteristics and related validation tests for measured product attributes”

Contents Highlights of Q2(R2) - (2)

- Validation tests and Methodology Evaluation
  - Specificity/Selectivity
  - Working range
  - Accuracy and Precision
  - Robustness

Contents Highlights of Q2(R2) - (3)

- Annex 1
  - Selection of validation tests based on objective of the analytical procedure
- Annex 2
  - Illustrated examples for frequently used analytical techniques and their validation requirements

Expected Benefits of Q2(R2)

- Encouragement of the use of more advanced analytical procedures leading to more robust quality oversight by pharmaceutical drug manufacturers
- Adequate validation data, resulting in reduction of information requests and responses, which can delay application approval
- Modernization of general methodology to include analytical procedures and data evaluation for biotechnological products and statistical/multivariate data evaluations
- Incorporation of the principles described in ICHQ8-Q10 which did not exist when Q2 (R1) was issued

Considerations

- The ICH Q14 and ICH Q2(R2) guidelines should be applied in conjunction with other existing and prospective ICH “Q” guidelines, including Q8–Q13.
- Analytical procedure development can be performed following a minimal or enhanced approach. Though not mandatory the use of individual elements of the enhanced approach is encouraged to be applied in an as needed basis.
- Tools and enablers discussed in ICH Q12 are applicable to analytical procedures, irrespective of the development approach.
- Examples in ICH Q2 Annex 2 describe common analytical technologies. The principles, however, can be applied in a similar fashion to other analytical technologies.

Conclusion

- The ICH Q14 and ICH Q2(R2) guidelines establishes harmonized scientific and technical principles for analytical procedure over the entire analytical procedure lifecycle.
- Applying principles described in ICH Q14 can improve regulatory communication between industry and regulators and facilitate more efficient, sound scientific and risk-based approval as well as post-approval change management of analytical procedures.
- ICH Q2(R2) will continue to provide a general framework for the principles of analytical procedure validation and has been modernized to include newer technologies (e.g., for biological products or multivariate analytical procedures).

Thank You!