FDA/CDER Perspectives on analytical procedure development and validation

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WCBP ICH Q14/Q2R2 Workshop
– Concepts and Enhanced Approaches to Analytical Procedure Lifecycle –
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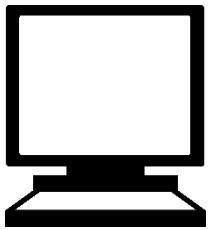
Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.



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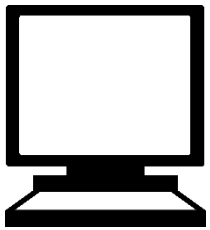



Drugs are no different.


FDA
Patients expect safe and effective medicine with every dose they take.

Pharmaceutical quality is

assuring *every* dose is safe and effective, free of contamination and defects.


It is what gives patients confidence
in their *next* dose of medicine.

Disclaimer

This presentation reflects the views of the author and should not be constructed to represent FDA's views or policies.

Outline

- FDA guidance documents and resources for analytical procedure development, validation and lifecycle management
- Common review issues with analytical procedures

FDA/CDER resources for analytical procedures development and validation

- FDA final guidance documents:
  "*Analytical Procedures and Methods Validation for Drugs and Biologics*", July 2015
  "*Q2(R1) Validation of Analytical Procedures: Text and Methodology*", September 2021*
  *This version combines Q2A (March 1995) and Q2B (May 1997) and is the same, in substance, as the ICH Q2(R1) guideline (November 2005).

- FDA draft guidance documents:
  "*Q2(R2) Validation of Analytical Procedures*", August 2022
  "*Q14 Analytical Procedure Development*", August 2022

- Office of Pharmaceutical Quality (OPQ) Emerging Technology Program (ETP):
  e.g., Process Analytical Technologies (PAT),
  Multi-Attribute Methods (MAM)

FDA guidance for reporting post-approval changes to an analytical procedure

- FDA final guidance "*Changes to an Approved Application for Specified Biotechnology and Specified Synthetic Biological Products",* July 1997

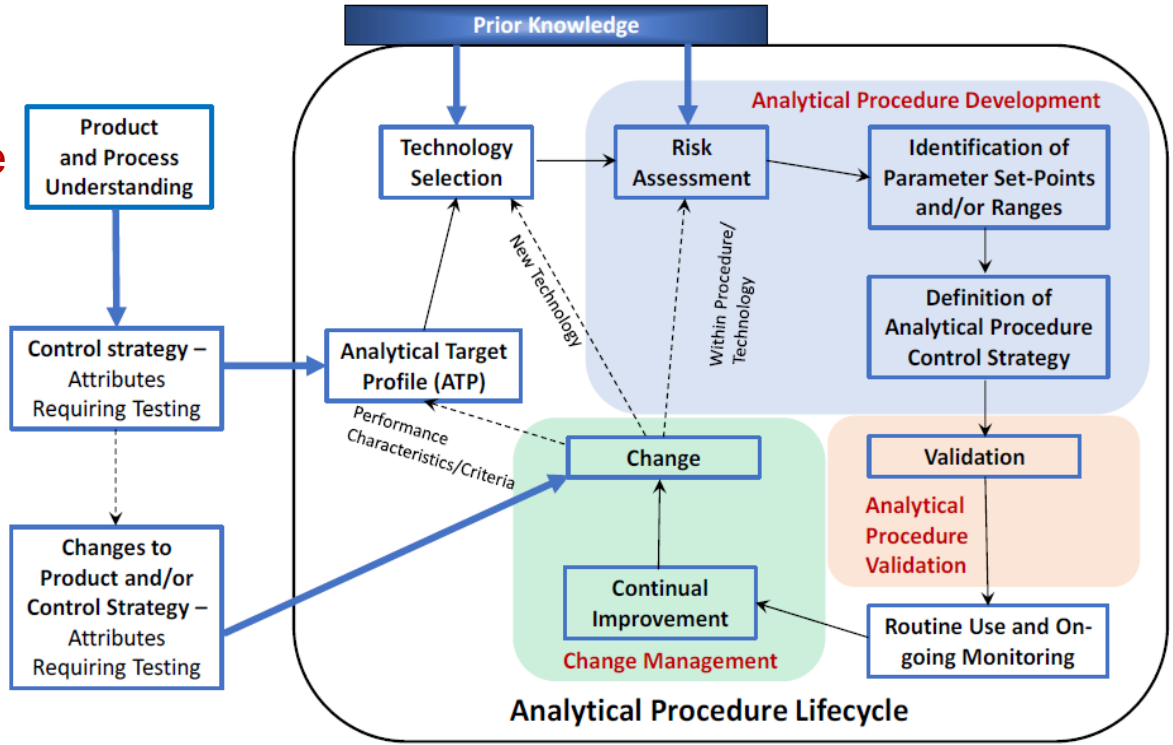
- FDA final guidance "*CMC Post-approval Manufacturing Changes for Specified Biological Products To Be Documented in Annual Reports*", December 2021.

New guidance for post-approval change management of analytical procedures

- FDA draft guidance: "*Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecyle Management*", May 2021; "*ICH Q12: Implementation Considerations for FDA-Regulated Products*", May 2021
- FDA draft guidance "*Q14 Analytical Procedure Development*", August 2022
- FDA final Guidance "*Comparability Protocols for Postapproval Changes to Chemistry, Manufacturing, and Controls Information in an NDA, ANDA, or BLA*", October 2022

Analytical Procedure Lifecycle

Quality Target Product Profile (QTPP)



Approaches:

- Minimal
- Enhanced

Q14 Analytical Procedure Development (Draft Guidance): ICH March 2022; FDA August 2022

Context of the new guidelines for analytical procedure

With ICH Q14, ICH Q2(R2), *etc.*, enhance transparency of scientific and regulatory expectations for information and data used to support development and lifecycle management of the existing and emerging analytical procedures.

- Minimal and enhanced approaches for analytical procedure development
- Analytical target profile (ATP)
- Analytical procedure control strategy
- Knowledge and risk management
- Established Conditions (ECs)
- Reporting postapproval changes
- In conjunction with ICH Q8-Q13

Comparability Protocols (CP) for proposed post-approval changes to an analytical procedure

A CP is a comprehensive, prospectively written plan for assessing the effect of a proposed post-approval CMC change(s) on the identity, strength, quality, purity, and potency of a drug product, for instance:

> *"For **replacement or modification of an existing analytical procedure** in an approved application, the new procedure must be scientifically sound and should **provide the same or greater assurance of product quality** than the currently approved procedure.*
>
> *The CP should include the **specific plan**, **description of statistical method(s) to be used**, and **acceptance criteria** to be achieved for evaluating the performance of the new procedure. **Method validation data** should be submitted with the notification of the change."*

Common review issues regarding analytical procedures and changes—1

- Unclear information on testing sites and analytical procedures

e.g., manufacturer information, method validation summary/report, Product Lifecycle Management (PLCM) document.

- Insufficient or inappropriate description of the analytical procedure and control strategy

e.g., dilution factor/scheme for each sample type,

cell culture conditions for cell-based assays,

method operation control ranges for which robustness results do not support.

Common review issues regarding analytical procedures and changes—2

- Insufficient information and data on validation of an analytical procedure to support 1) changes in the analytical procedure; 2) changes in test sites

e.g., summary of changes and bridging studies if applicable,

type of samples (e.g., in-process, non-degraded, degraded, spiked) used for validation/transfer to support the suitability of methods for the intended purpose(s),

adequacy of validation experiments performed when transferring analytical procedures to a different laboratory.

How will the new version of Q2 and the new Q14 guidelines help?

- Include general considerations for development, validation and lifecycle management of analytical procedure for the assessment of quality of drug substance and drug product.

- Facilitate communication between industry and regulators, e.g., on topics related to how to justify the analytical procedure control strategy

Acknowledgement

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