U.S. FOOD & DRUG ADMINISTRATION

Q2(R2)/Q14, Revision of Q2(R1) Analytical Procedure Validation and Analytical Procedure Development

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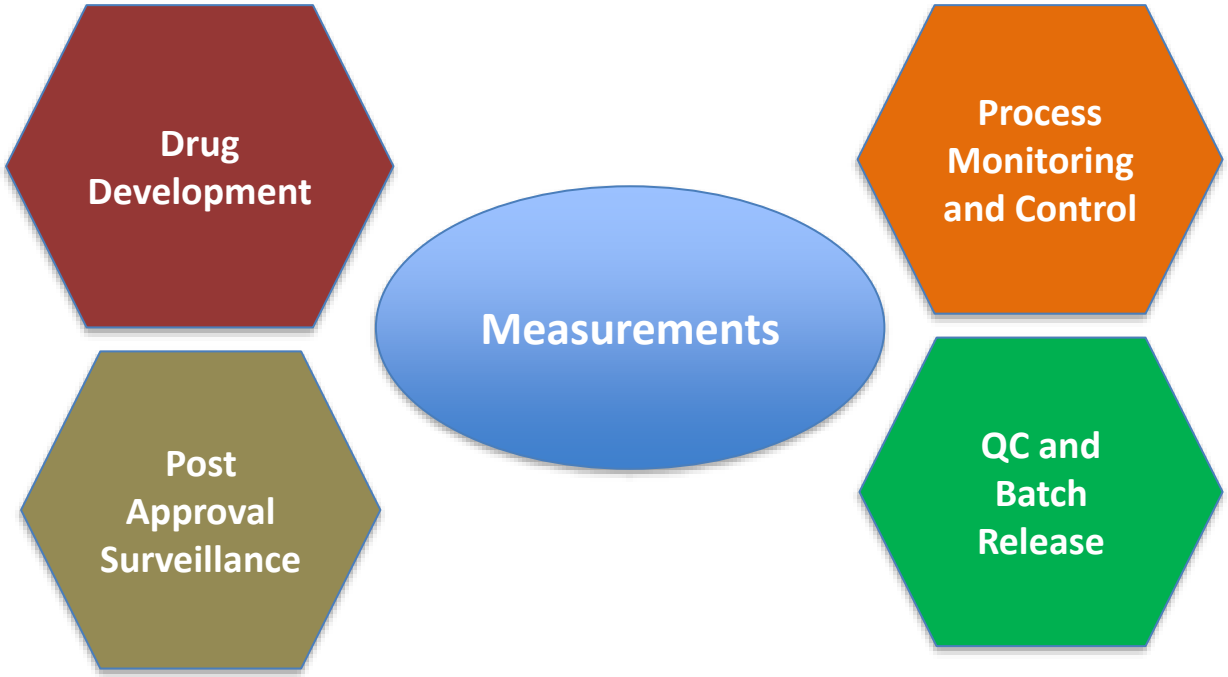
Everyone deserves confidence in their *next* dose of medicine.

Pharmaceutical quality assures the availability, safety, and efficacy of *every* dose.

What Do We Want?

- Fewer Failures
- Minimize/Eliminate Recalls
- Regulatory Flexibility (fewer filings)
- Lower Barriers for New Analytical Technology
- Quality Drugs for Consumers

The Central Science?



How Do ICH Guidelines Help?

- Standardize
  - Provide guidance on the content of sections of the Common Technical Document.
- Harmonize/Harmonise
  - Common requirements globally.
- Framework
  - Adaptable to technological change.
  - Allows continuous improvement.

Q2(R1) Was Finalized In The 90's

- Scientific and technological progress has been made since the document was written
- Advanced therapies are in drug development and commercialization
- Associated analytical techniques are multiplying
  - hyphenated techniques (LC-MS) or spectroscopic approaches that are multivariate (*e.g.*, NIR, Raman)

Q2: The Issue and Costs

- Q2(R1) not directly applicable to multivariate spectroscopy data.
  - Lack of clear guidelines leads to inadequate validation data in regulatory submissions.
    - Recursive information requests and responses.
- NIR commonly used for real time release testing.
  - A barrier to innovation in analytical approaches for pharmaceutical quality assessment.

Q14: The Issue and Costs

- No ICH Guideline on Analytical Procedure Development
  - Applicants rarely present performance evaluations.
    - Can lead to recursive regulatory communication around non-conventional analytical procedures.
      - *e.g.*, PAT driven multivariate models used for process control.
  - Impedes applicants from presenting a scientific basis (*e.g.,* QbD data) for regulatory flexibility for post-approval analytical procedure changes.
- Delayed access to medication and increased cost

What is Developed is Validated

Objectives / Performance Characteristics
Analytical Procedure
Related information from Development

Analytical Procedure
Lifecyle Management

Q14

Q2

Validation protocol

Validation report

Plan for validation strategy:

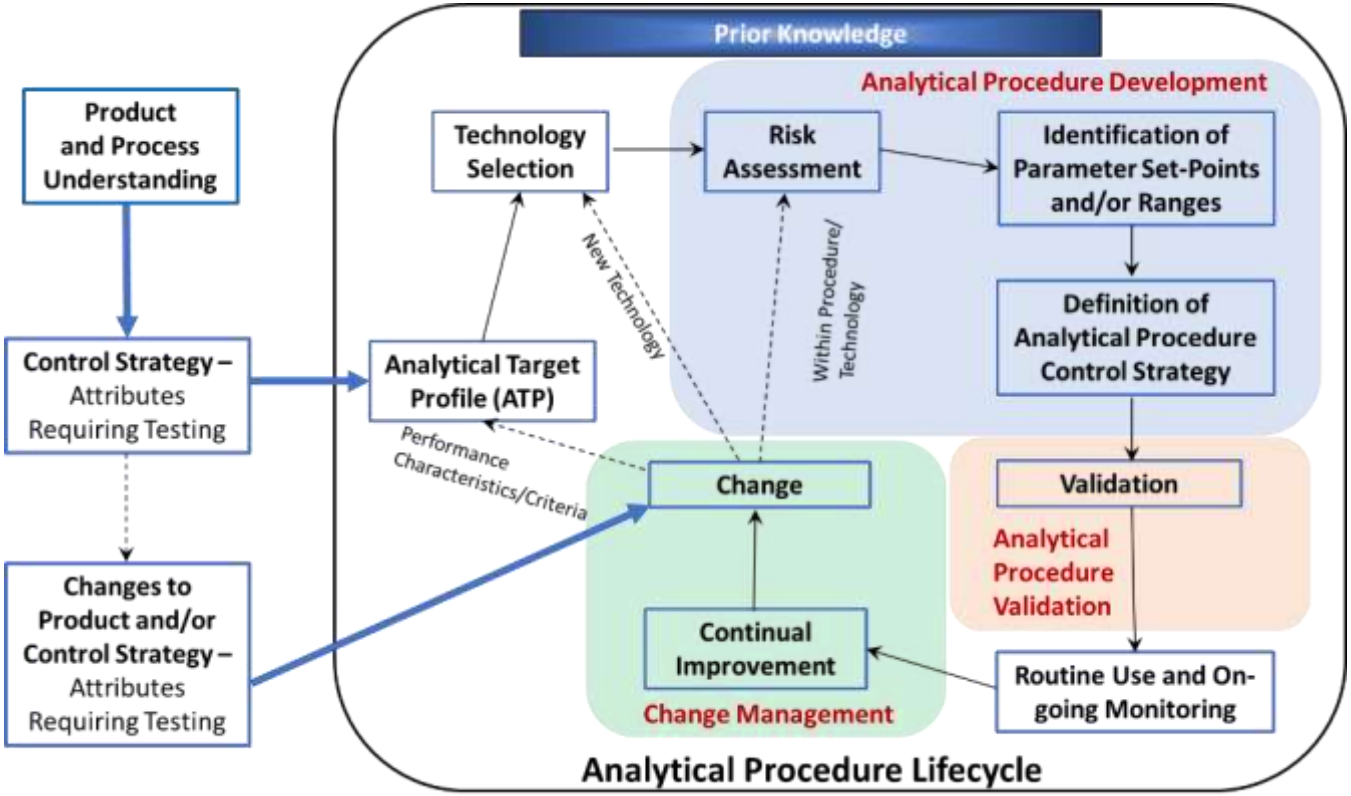
- Evaluation of existing development or validation data with justification
- Additional experiments and evaluation according Q2 (standard) methodology or alternative approach with justification

Document validation results and Data:

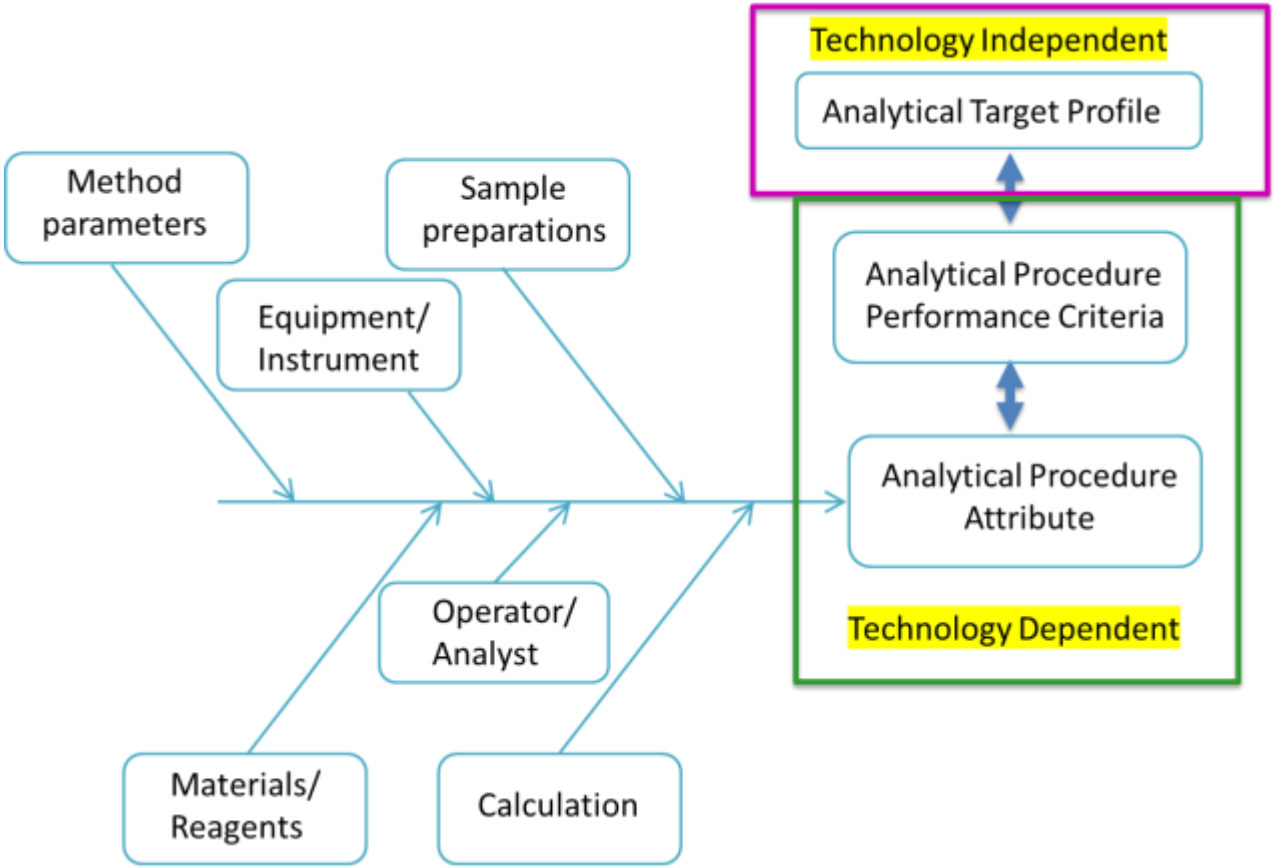
- Evaluation against Acceptance Criteria or Parameter Ranges
- Conclusions and acceptance of analytical procedure performance

Experiments and/or Evaluation of data

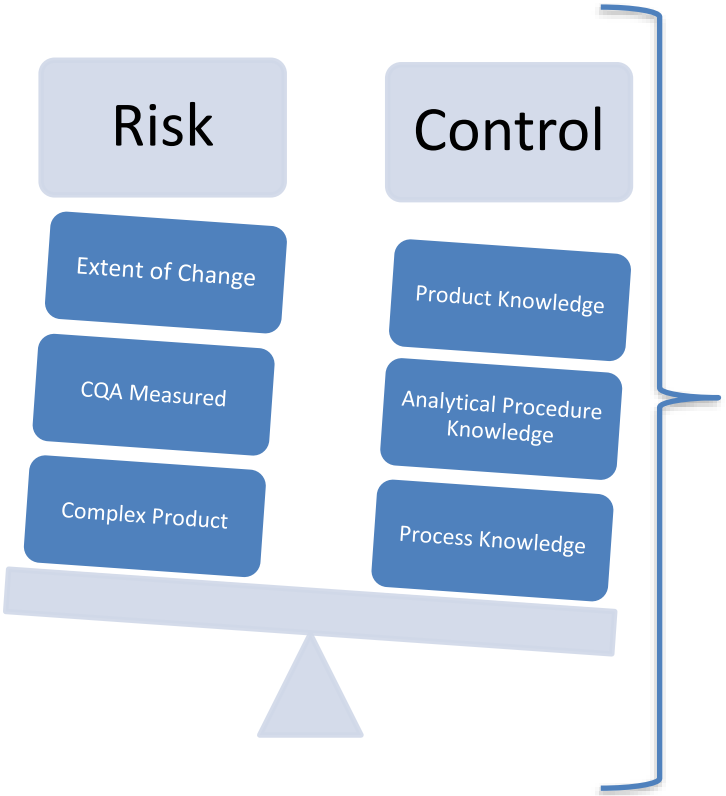
Analytical Procedure Lifecycle



Knowledge, Risk and ATP



Change, Risk and Reporting



Reporting Category agreement with regulator using Q12 tools

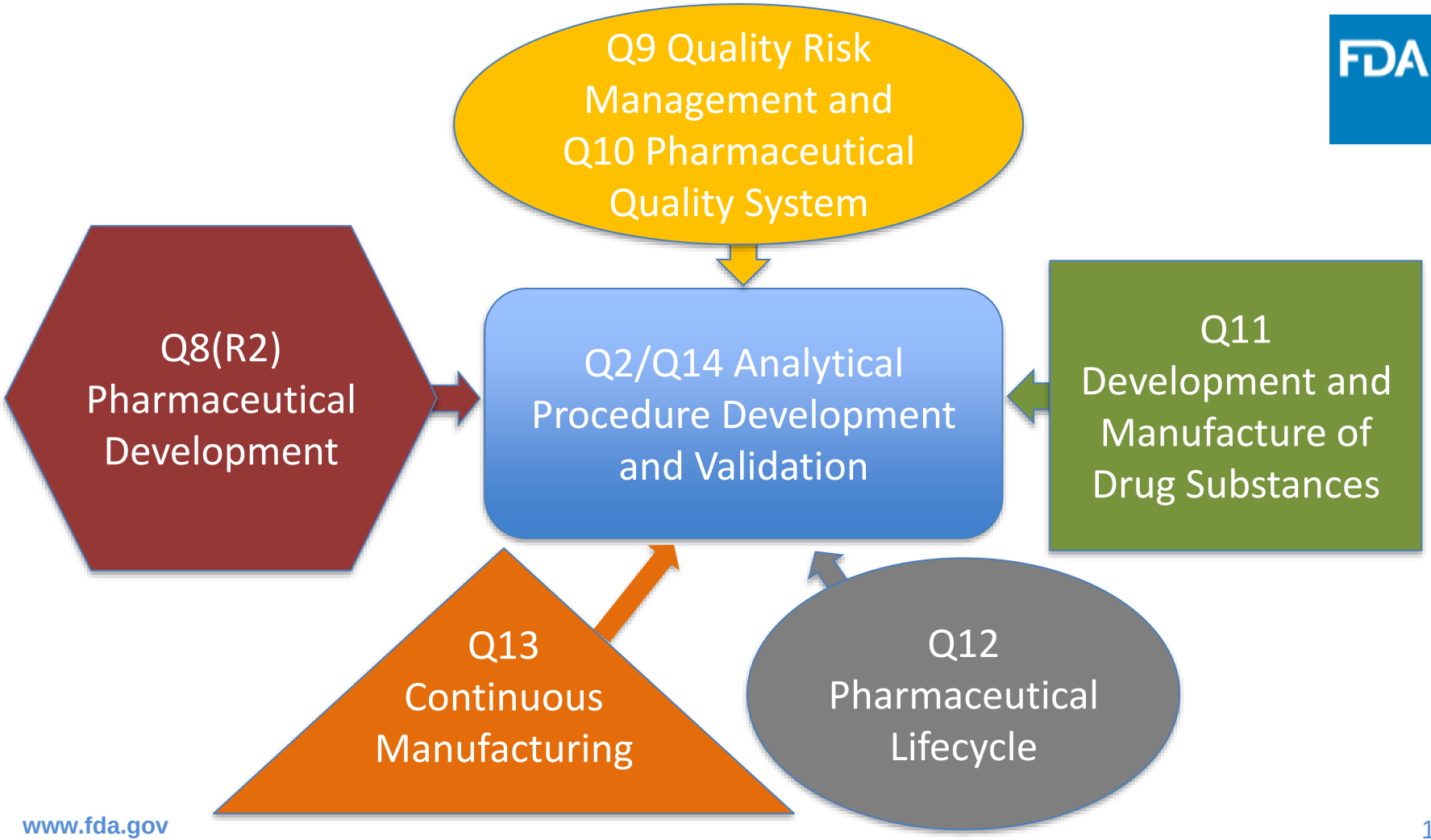
High

Med

Low

ICH Q2(R2) and Q14

- Reached Step 4 in November 2023
- Together ICH Q14 and ICH Q2(R2) describe the development and validation of analytical procedures used for the assessment of drug substance and drug product quality.
- ICH Q14 describes the scientific principles for development, change management and submission of analytical procedures using minimal or enhanced approaches.
- ICH Q2(R2) provides guidance for establishing and submitting evidence that an analytical procedure is fit for assuring drug quality.


Q9 Quality Risk Management and Q10 Pharmaceutical Quality System
Q8(R2) Pharmaceutical Development
Q2/Q14 Analytical Procedure Development and Validation
Q11 Development and Manufacture of Drug Substances
Q13 Continuous Manufacturing
Q12 Pharmaceutical Lifecycle

Questions?

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