2025 ICH Q2(R2)/Q14 Training based on Training Materials

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The goals of this presentation is to help the audience

1 Understand Overall structure of Q2(R2) and Q14

2 Find point/theme of interest

By presenting

Overall structure of Q2 and Q14 guidelines and selected slides from the training materials.

This presentation contains the presenter's personal opinion and does not represent the formal ICH position nor the formal MHLW's position.

Outline of This Presentation

- **Overview of the two guidelines**

- Structure of the training materials and read suggestions

- Key points with examples/cases

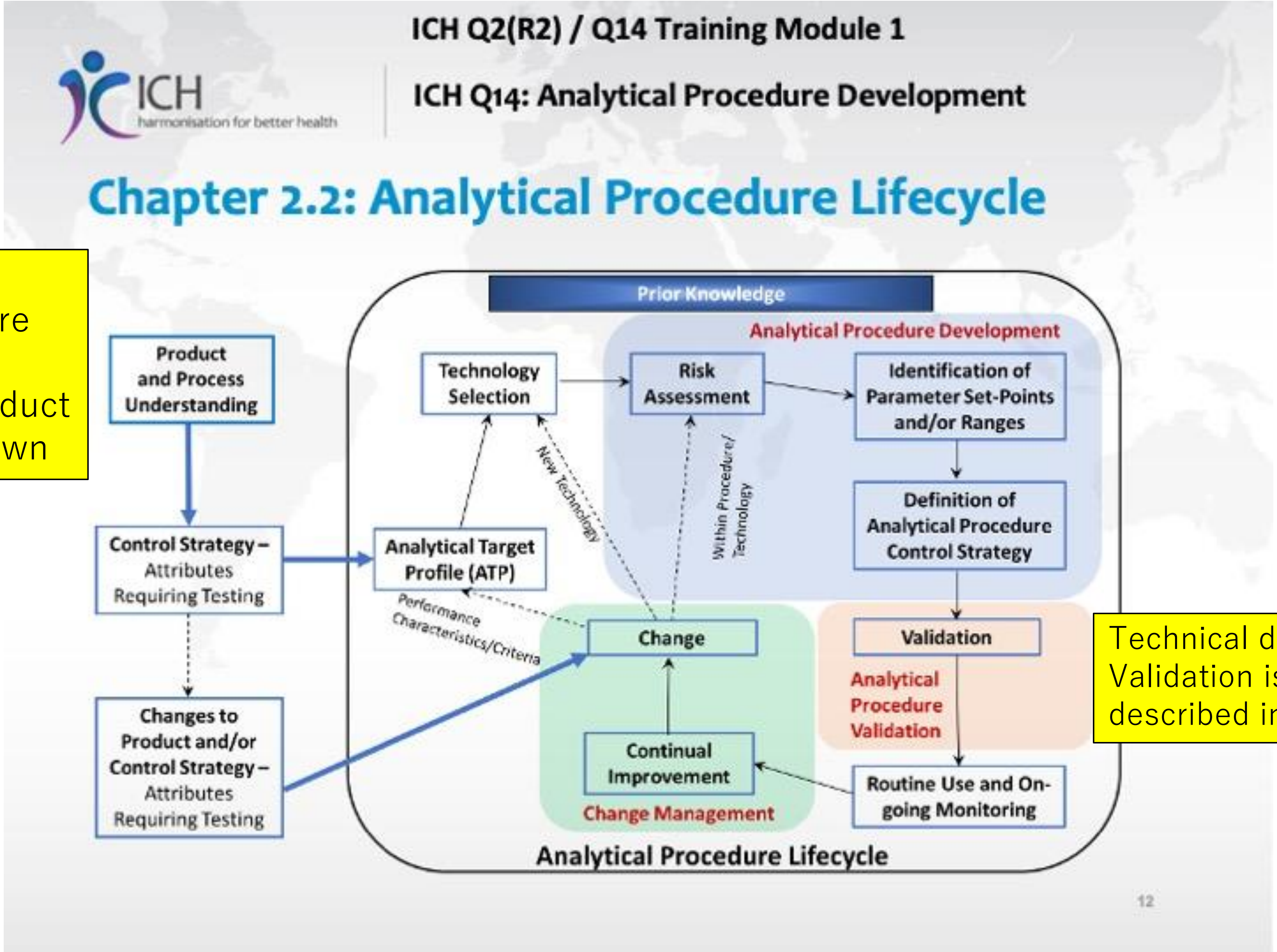
Validation study vs. Validation test (Validation strategy, Development data, MODR, Platform)

Lifecycle(ATP, Development, Validation, ECs, Changes) example(s)

- Conclusions

Q14 has
this lifecycle figure

Key points in product development shown

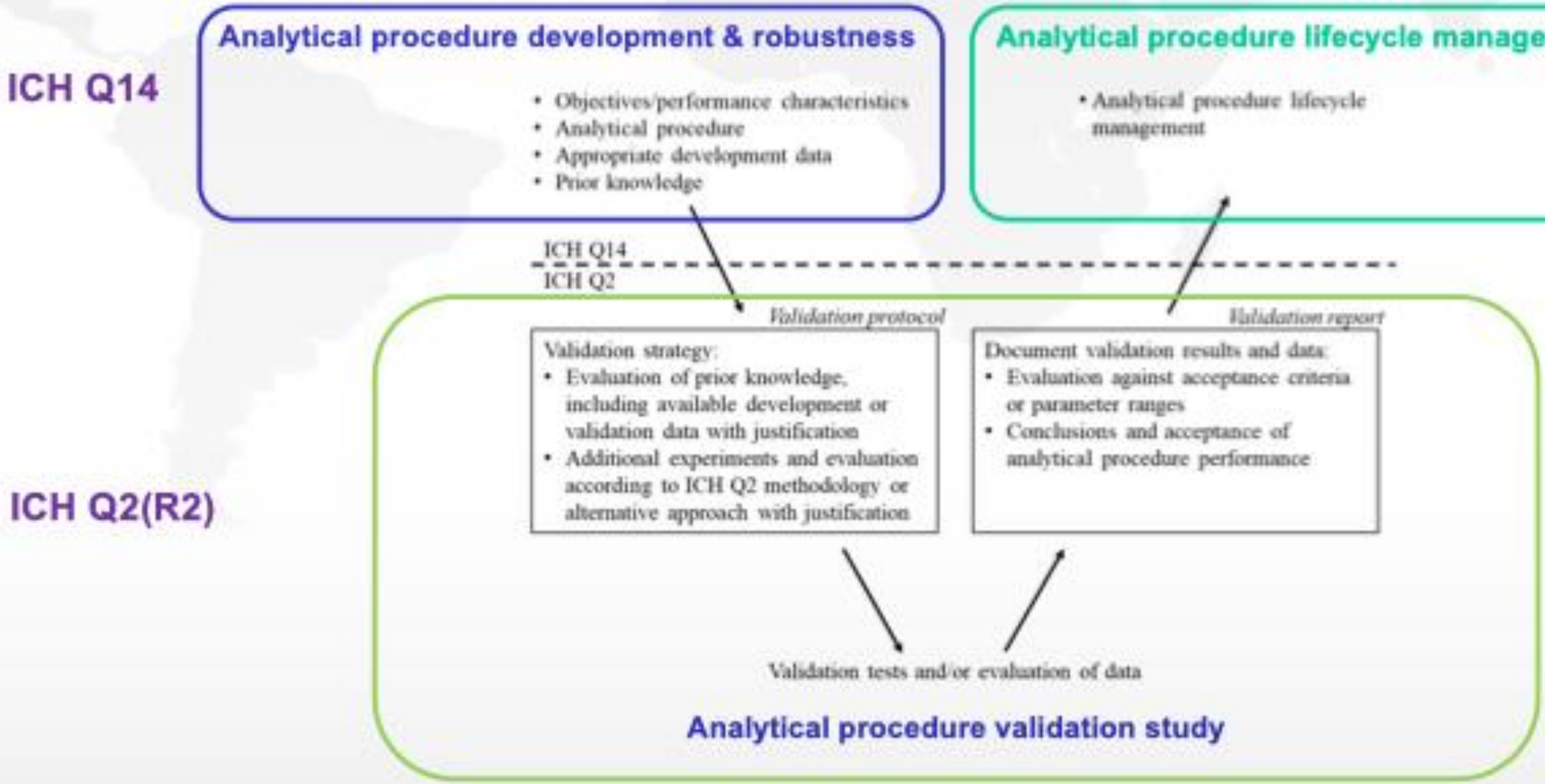


Technical details of Validation is described in Q2

ICH Q2(R2) / Q14 Training Module 2

Analytical Procedure Lifecycle

- **ICH Q2(R2) analytical procedure validation is an element of the analytical procedure lifecycle described in ICH Q14**



Adapted from ICH Q2(R2) Figure 1: Validation study design and evaluation

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Q2 has this chart showing linkage between development and validation

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- Conclusions

ICH Q2(R2) / Q14 Training Modules
Map of Contents

High level of cross linkage

	Module Number	Q2(R2) Q14	Contents			Linkage Cross Reference
41	Module 1	Q2(R2)/ Q14	**Step 4 Presentation for ICH Q2(R2) and ICH Q14**			
33	Module 2	Q2(R2)	**Fundamental principles of ICH Q2(R2)**			
			Part A	Analytical Procedure Validation Strategy		Module 3 Part B Use of development data Module 4 Part B, Part E and Part F Module 7 MODR
			Part B	Details of Validation Terms		
			Part C	Combined Accuracy and Precision		Module 3 Part B Use of Confidence Intervals
			Part D	Considerations when Setting Performance Criteria		
102	Module 3	Q2(R2)	**Practical Applications of ICH Q2(R2)**			
			Part A	ICH Q2(R2) Annex 1 and 2	Table 3 Separation techniques	
					Table 5 Dissolution with HPLC	Module 5 Part E
					Table 8 Quantitative PCR	
					Table 9 Particle size measurement	
			Part B	Other Validation Topics	Platform Analytical Procedures	Module 7 Platform Analytical Procedures
					Use of Confidence Intervals	
					Use of Replicates	
					Use of Development Data	
					Single Point Calibration	
					Extrapolation of Validation Range	
					Quantitative Test vs. Limit Test	Module 5 Part E
46	Module 4	Q14	**ICH Q14 General Considerations**			
			Part A	Minimal and Enhanced Approach		
			Part B	Analytical Procedure Lifecycle		
			Part C	Analytical Target Profile (ATP)		
			Part D	Risk Assessment in Analytical Procedure Development		Module 5 Part C Module 7
			Part E	Robustness and Parameter Ranges		Module 2 Part A Module 7 MODR
			Part F	Analytical Procedure Control Strategy		Module 2 Part A Module 7

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High level of cross linkage

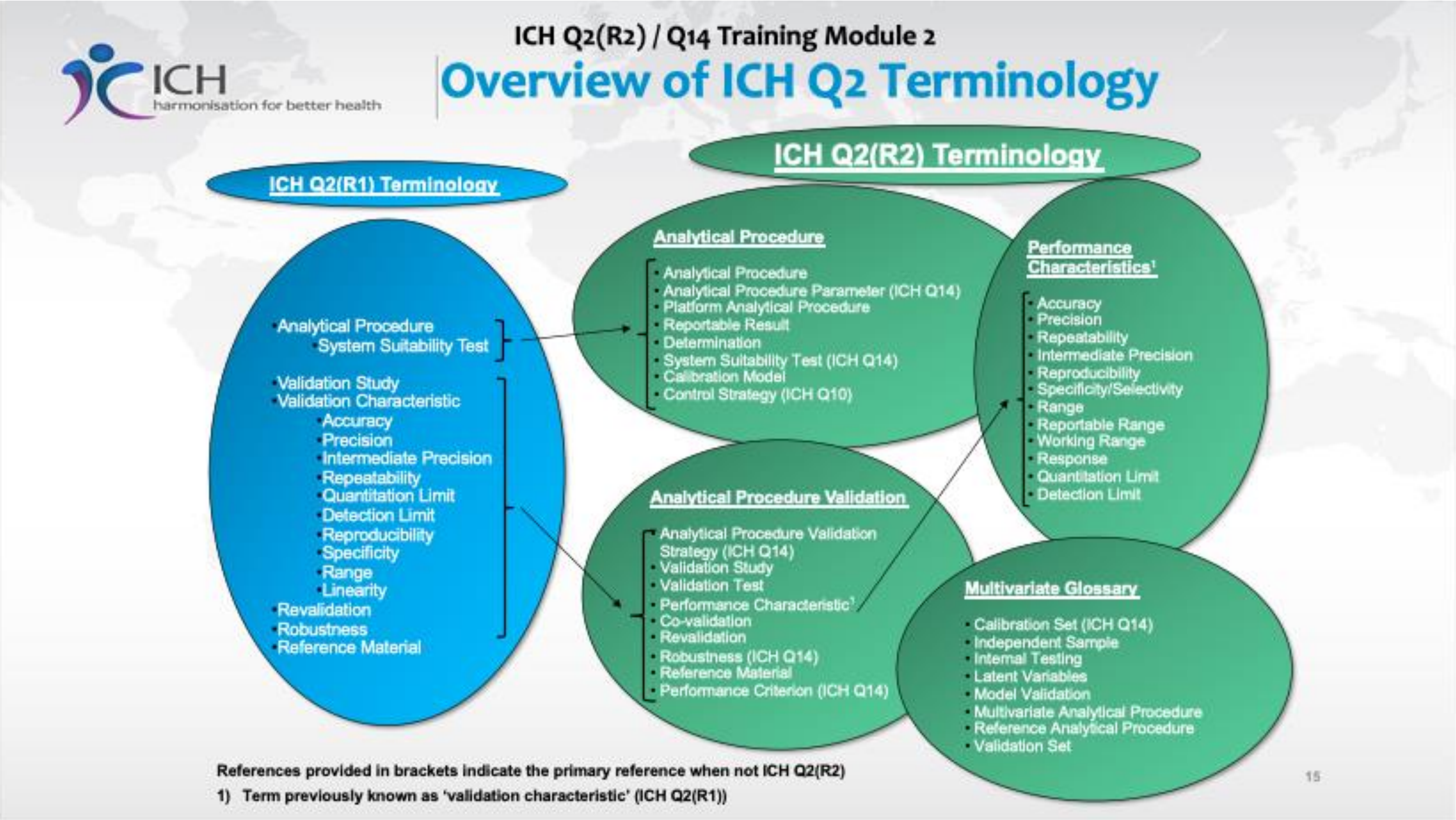
	Module Number	Q2(R2) Q14	Contents		Linkage Cross Reference
60	Module 5	Q14	**Further Concepts in ICH Q14**		
			Part A	Established Conditions and the Link to ICH Q12	Module 7
			Part B	Change Management: Identification of ECs/Reporting Categories and the Use of the Decision Tree	Module 7
			Part C	Knowledge and Risk-based Change Management	Module 4 Part D
			Part D	Explanation of ICH Q14 Tables 1 and 2, Implementation of Changes, and Bridging Studies	
			Part E	Submission Requirements in ICH Q14 Chapter 10	Module 3 Part A (Table 5) Module 6 Module 7 and Module 7 NIR
31	Module 6	Q2(R2)/ Q14	**Multivariate Analytical Procedure**		
			Introduction		
			Examples	Raman spectroscopy for identity testing	
				NIR for assay	Module 5 Part E Module 7 NIR
				Raman spectroscopy for glucose testing	
88p	Module 7	Q2(R2)/ Q14	**Additional Case Studies and Examples**		
			Impurity	Case Study - Measurement of Stereoisomers as Specific Process Related Impurities in a Small Molecule Drug Substance	
			Potency	Case Study - Measurement of Potency for an anti-TNF-alpha Monoclonal Antibody	
			MAM	Case Study - MAM by Peptide Mapping LC-MS	
			NIR	Case Study - At-line Assay of Core Tablets by Multivariate Analytical Procedure in Continuous Manufacturing of a Drug Product	Module 5 Part E Module 6
			Platform Analytical Procedures	Example - Platform Analytical Procedure, Determination of High Molecular Weight Species in Monoclonal Antibody Products	Module 3 Part B Platform Analytical Procedures
			MODR	Example - Application of the Enhanced Approach Using DoE Studies - Establishment and Validation Options for MODRs	Module 2 Part A Module 4 Part E

NIR: Near-infrared spectroscopy
MAM: Multi-attribute Methods
MODR: Method Operable Design Region

Read Suggestions

- If you need only a very high level understanding on Q2 and Q14, look at training module 1.
- If you like to get comprehensive detail understanding, pick one of four case studies in module 7 and read corresponding descriptions module 2 through 6.

- Terms used in the guidelines are mostly defined. For clear understanding of those, check definitions first. Also, interrelations between those terms are important in order to understand the contents, the following figure and chart may be useful.


ICH
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ICH Q2(R2) / Q14 Training Module 2
Overview of ICH Q2 Terminology
ICH Q2(R1) Terminology
•Analytical Procedure
•System Suitability Test
•Validation Study
•Validation Characteristic
•Accuracy
•Precision
•Intermediate Precision
•Repeatability
•Quantitation Limit
•Detection Limit
•Reproducibility
•Specificity
•Range
•Linearity
•Revalidation
•Robustness
•Reference Material
ICH Q2(R2) Terminology
Analytical Procedure
• Analytical Procedure
• Analytical Procedure Parameter (ICH Q14)
• Platform Analytical Procedure
• Reportable Result
• Determination
• System Suitability Test (ICH Q14)
• Calibration Model
• Control Strategy (ICH Q10)
Performance Characteristics[1]
• Accuracy
• Precision
• Repeatability
• Intermediate Precision
• Reproducibility
• Specificity/Selectivity
• Range
• Reportable Range
• Working Range
• Response
• Quantitation Limit
• Detection Limit
Analytical Procedure Validation
• Analytical Procedure Validation Strategy (ICH Q14)
• Validation Study
• Validation Test
• Performance Characteristic[1]
• Co-validation
• Revalidation
• Robustness (ICH Q14)
• Reference Material
• Performance Criterion (ICH Q14)
Multivariate Glossary
• Calibration Set (ICH Q14)
• Independent Sample
• Internal Testing
• Latent Variables
• Model Validation
• Multivariate Analytical Procedure
• Reference Analytical Procedure
• Validation Set
References provided in brackets indicate the primary reference when not ICH Q2(R2)
1) Term previously known as 'validation characteristic' (ICH Q2(R1))
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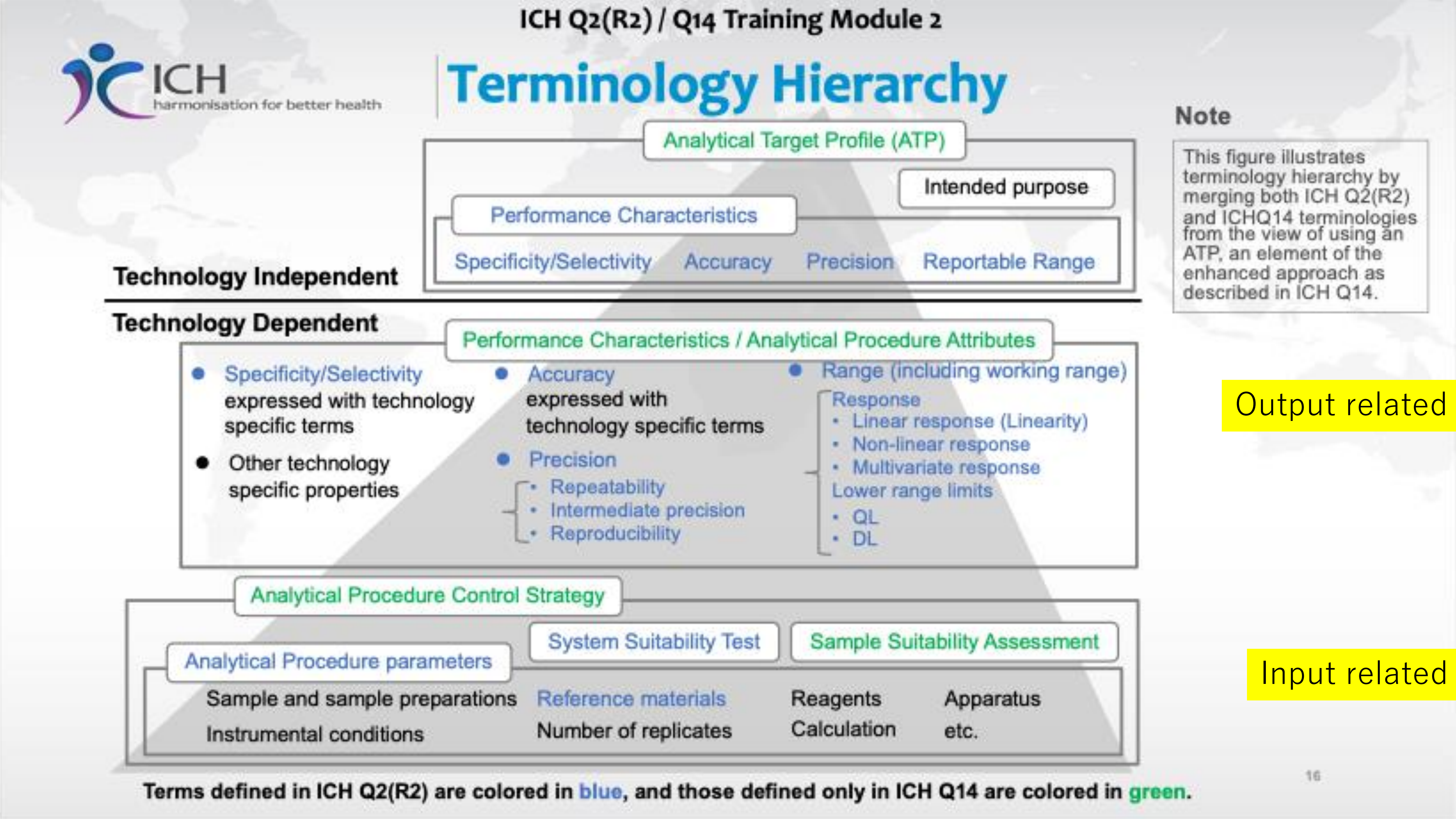
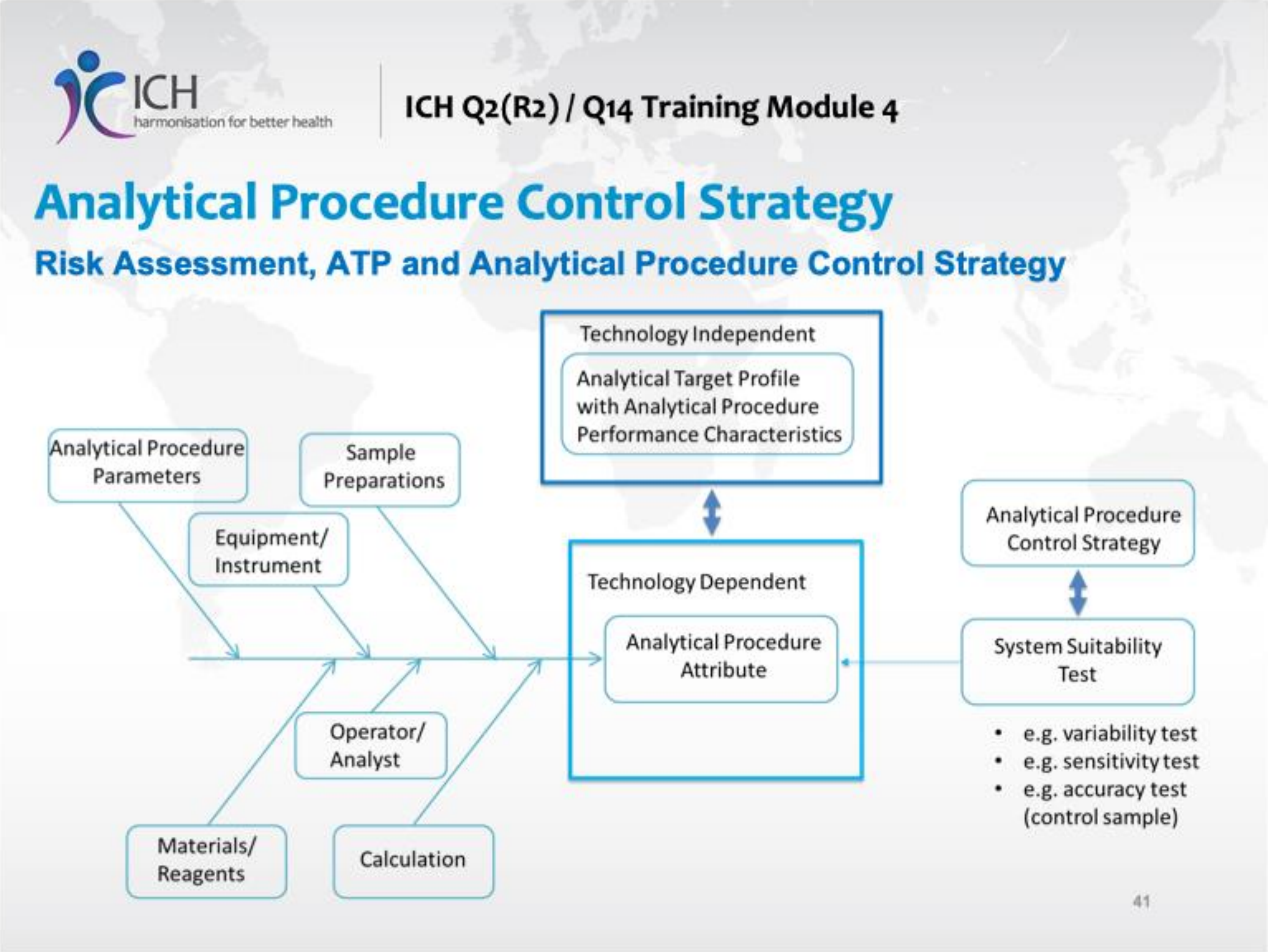


Output related

Input related


ICH
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ICH Q2(R2) / Q14 Training Module 4
Analytical Procedure Control Strategy
Risk Assessment, ATP and Analytical Procedure Control Strategy
Technology Independent
Analytical Target Profile with Analytical Procedure Performance Characteristics
Analytical Procedure Parameters
Sample Preparations
Equipment/ Instrument
Technology Dependent
Analytical Procedure Attribute
Analytical Procedure Control Strategy
System Suitability Test
Operator/ Analyst
Materials/ Reagents
Calculation
• e.g. variability test
• e.g. sensitivity test
• e.g. accuracy test (control sample)
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ICH Q2(R2) / Q14 Training Module 2

Analytical Procedure Development Flow in Line with ICH Q14

Analytical Target Profile (ATP)
Consisting of below elements
- Intended purpose of analytical procedure
- Details on quality attribute to be tested
- Performance characteristics and associated performance criteria

Technology selection

Analytical procedure development

Risk assessment: Identifying analytical procedure parameters with potential impact on performance, assessing the potential impact, and identifying analytical procedure parameters to be investigated experimentally.

Robustness evaluation: Testing by deliberate variations of analytical procedure parameters considering duration of analysis.

Analytical procedure parameter ranges: Investigating the impact of analytical procedure parameter (input) ranges to analytical procedure attributes (output) and associated criteria that can be derived from an ATP.

Analytical procedure control strategy: Includes analytical procedure parameters needing control and SST. SST is designed to verify selected analytical procedure attributes.

Validation study

Validation protocol : A written plan describing the analytical procedure to be validated, performance characteristics / analytical procedure attributes and associated criteria derived from an ATP, validation tests to be conducted, participating sites etc. Validation protocol is designed based on or includes analytical procedure validation strategy considering prior knowledge and existing data.

Validation tests and/or evaluation of data

Validation report: Document of validation results and data; and conclude suitability

Note

When using an ATP a "Performance characteristic" is a technology-independent description of characteristic with an associated and defined acceptance criteria. Once a technology is selected, technology-dependent performance characteristics can be determined, which are defined as "Analytical Procedure Attributes" in ICH Q14.

VALIDATION STUDY

An evaluation of **prior knowledge, data, deliberate experiments**

VALIDATION TEST

Validation tests are **deliberate experiments**

Terms defined in ICH Q2(R2) are colored in blue, and those defined only in ICH Q14 are colored in green.

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Lifecycle(ATP, Development, Validation, ECs, Changes) example(s)

- Conclusions

ICH Q2(R2) / Q14 Training Module 2

Analytical Procedure Validation Study

Documented study designed to provide sufficient evidence that the analytical procedure meets its objectives

- **Protocol:**
  - Intended purpose of the analytical procedure
  - Based on the intended purpose, provide the appropriate *Performance Characteristics* to be validated (as per ICH Q2(R2) Table 1) and the associated *Performance Criteria*
  - Overview of analytical procedure validation strategy
    - Justification of appropriateness of any prior knowledge
      - "Suitable data derived from development studies can be used as part of validation data" (ICH Q2(R2))
      - "In cases where prior knowledge is used (e.g., from development or from previous studies), appropriate justification should be provided" (ICH Q2(R2))
      - See also Module 3, Part B (Use of Development Data)
    - Experimental design to assess performance characteristics for which suitable prior knowledge is not sufficient or is not available.
      - Experimental design should reflect the number of replicates used in routine analysis to generate a reportable result. If justified, it may be acceptable to perform some validation tests using a different number of replicates or to adjust the number of replicates in the analytical procedure based on data generated during validation.
- **Report**
  - Results of the study, including comparison to Performance Criteria
  - A tabular validation summary to demonstrate ICH Q2(R2) compliance may be useful
  - A conclusion regarding the suitability of the procedure for it's intended use should be included

VALIDATION STUDY

An evaluation of

prior knowledge, data , deliberate experiments

VALIDATION TEST

Validation tests are

deliberate experiments

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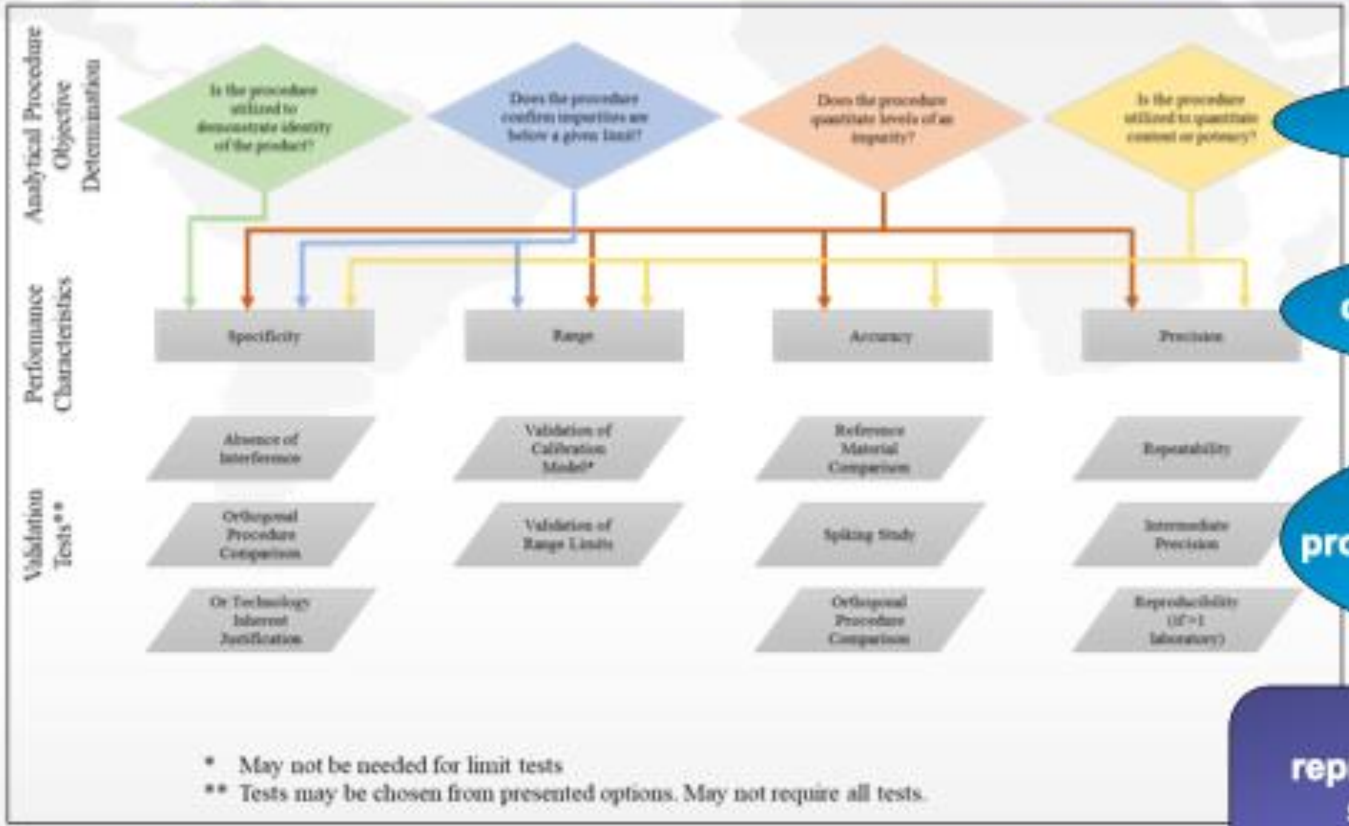
ICH Q2(R2) Framework

ICH Q2(R2) provides a framework for the approach to analytical procedure validation, which can be applied irrespective of the measured quality attribute or the technology used.



ICH Q2(R2) Figure 2: Examples of relevant validation tests based on the objective of the analytical procedure

Objectives of the analytical procedure are determined

Relevant performance characteristics are selected based upon the intended use of the analytical procedure

Suitable validation test(s) are chosen based on specific procedure and product considerations, *e.g.*, available reference materials, inherent properties of the technology used.

Figure 2 (Annex 1) provides a flow chart representation of the performance characteristic selection from Table 1, as well as example validation tests that may be considered for each characteristic.

ICH Q2(R2) / Q14 Training Module 1

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ICH Q2(R2): Validation of Analytical Procedures

Annex 2 - Illustrative Examples for Analytical Techniques

Specific non-binding examples for common techniques :

- Separation techniques (*e.g.*, HPLC, GC, CE) for impurities or assay
- Separation techniques with relative area quantitation, (*e.g.*, product-related substances such as charge variants)
- Elemental Impurities by ICP-OES or ICP-MS
- Dissolution with HPLC as product performance test for an immediate release dosage form
- Quantitative ^{1}H-NMR (internal standard method) for the assay of a drug substance
- Binding assay (*e.g.*, ELISA, SPR) or cell-based assay for determination of potency relative to a reference
- Quantitative PCR (quantitative analysis of impurities in drug substances or products)
- Particle size measurement (dynamic light scattering; laser diffraction measurement) as a property test
- NIR analytical procedure for core tablet assay
- Quantitative LC/MS analysis of trace impurities in product

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This Annex gives different **evaluation** types for **Performance Characteristics**

The dissolution example uses development data for specificity

The qNMR example employs calibration for precision

ICH Q2(R2) / Q14 Training Module 3

ICH Q2(R2) Annex 2 Examples

- The tables presented in ICH Q2(R2) Annex 2 provide example approaches for analytical procedure validations.
  - The technologies and approaches presented were constructed to illustrate potential applications of the principles contained within the guideline and are not exhaustive.
  - The examples in Annex 2 are not intended to be mandatory, and alternative approaches (fulfilling the intent of the guideline) may also be acceptable.
- Examples have been elucidated for four of the technologies contained in the tables in Annex 2.
  - These examples provide an additional layer of information beyond that in Annex 2, and exemplify the data which may be collected during analytical procedure validation.
  - This additional information is not intended to be mandatory, and alternative approaches (fulfilling the intent of the guideline) may also be acceptable.
- The following slides present example validation data relating to:
  - ICH Q2(R2) Annex 2, Table 3:
    - Separation techniques with relative area quantitation (e.g., product-related substances such as charge variants).
  - ICH Q2(R2) Annex 2, Table 5:
    - Dissolution with high-performance liquid chromatography (HPLC) as product performance test for an immediate release dosage form.
  - ICH Q2(R2) Annex 2, Table 8:
    - Quantitative polymerase chain reaction (qPCR) (quantitative analysis of impurities in drug substances or products).
  - ICH Q2(R2) Annex 2, Table 9:
    - Particle size measurement (dynamic light scattering; laser diffraction measurement) as a property test.

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Example Validation Data for Separation Techniques with Relative Area Quantitation (Annex 2, Table 3)

Technique	Separation techniques with relative area quantitation, (e.g., product-related substances such as charge variants)
Performance characteristic	**Validation study methodology**
Specificity / Selectivity	Absence of relevant interference: With product, buffer, or appropriate matrix, and between individual peaks of interest Demonstration of stability-indicating properties through appropriate forced degradation samples if necessary
Precision	Repeatability: Replicate measurements with 3 times 3 levels across the reportable range or 6 times at 100% level, considering peak(s) of interest Intermediate precision: e.g., different days, environmental conditions, analysts, equipment
Accuracy	Comparison with an orthogonal procedure and/or suitably characterised material (e.g., reference material) or Accuracy can be inferred once precision, linearity and specificity have been established. or Spiking studies with forced degradation samples and/or suitably characterised material
Reportable Range	Validation of calibration model across the range: Linearity: Between measured (observed) relative result versus theoretically expected relative result across specification range(s), e.g., by spiking or degrading material Validation of lower range limits: QL (and DL) through a selected methodology (e.g., signal-to-noise determination)
Robustness and other considerations (performed as part of analytical procedure development as per ICH Q14)	Deliberate variation of relevant parameters, e.g., Sample preparation: extraction volume, extraction time, temperature Separation parameters: column/capillary lot, mobile phase/buffer composition and pH, column/capillary temperature, flow rate, detection wavelength Stability of sample and reference material preparations **Relative Response Factors** If the analyte has a different response from the reference material (e.g., a different specific UV absorbance), relative response factors should be calculated using the appropriate ratio of responses. This evaluation may be performed during validation or development, and should use the finalised analytical procedure conditions and be appropriately documented If the relative response factor is outside the range 0.8-1.2, then a correction factor should be applied. If an impurity/degradation product is overestimated, it may be acceptable not to use a correction factor

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The bottom box is included in Q2 after debate by the E W G

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Determination of Monoclonal Antibody Charge Variants by Ion Exchange Chromatography

Liquid Chromatography (LC) procedure

- Column: weak cation-exchange resin, 250 mm × 4.0 mm (10 µm)
- Gradient elution: mobile phase A (phosphate buffer), mobile phase B (phosphate buffer, sodium chloride)
- Sample concentration: 1 mg/mL

Parameter	Set point
Flow rate	1.0 mL/min
Column temperature	40°C
Detection	Ultraviolet (UV) at 280 nm
Run time	80 min
Injection volume	50 µL

Acceptance criteria defined for % acidic peaks, % main peak, % basic peaks.

Other performance Characteristics
are shown in the module.
But not shown in
this presentation

ICH Q2(R2) / Q14 Training Module 3

Specificity

Sample matrix interference

Analyse the separation and matrix component interference of the drug substance (DS).

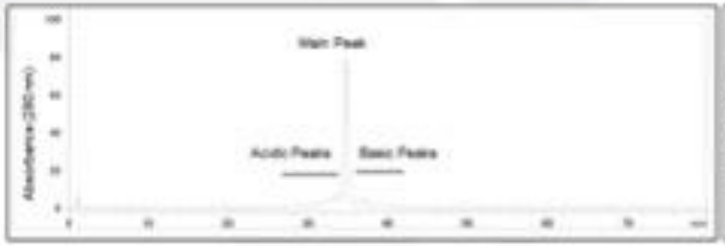
- DS shows clear separation order of acidic peaks, main peak and basic peaks.
- No significant interference from sample matrix components in the chromatographic region of interest.

Stability-indicating properties

Comparison of chromatograms obtained with reference material and stressed sample.

- The chromatogram of the reference material should be distinguishable from that of stressed sample by visual comparison.

Chromatogram of the DS



Chromatogram for DS formulation buffer

Relative peak area (%)

	Acidic peaks			Main peak	Basic peaks	
	Peak 1	Peak 2	Peak 3	Peak 4	Peak 5	Peak 6
Reference material	2.23	9.88	12.00	65.17	8.85	1.86
Stressed sample	3.55	11.00	11.66	46.82	11.54	3.35

Additional new peaks*: Relative peak area (%)

	Peak 7	Peak 8	Peak 9	Peak 10	Peak 11	Sum
Stressed sample	1.78	1.03	3.56	2.63	2.98	12.08

**Table contains extra peaks labelled independently on whether the new peaks are acidic or basic peaks*

ICH Q2(R2) / Q14 Training Module 3

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Use of Development Data as part of Validation Data

The ICH Q2(R2) defines the following:

From Chapter 2 "General Considerations for Analytical Procedure Validation": "Suitable data derived from development studies (see ICH Q14) can be used as part of validation data".

From Chapter 2.1 "Analytical Procedure Validation Study": "In cases where prior knowledge is used (e.g., from development or from previous studies), appropriate justification should be provided".

Prior knowledge and/or data generated during development, e.g., while establishing proven acceptable ranges (PAR) or method operable design regions (MODR), can be used as part of the validation study.

MODR is explained in modules 2, 4 and

The broader the prior knowledge and the knowledge about the relationship between analytical parameters and analytical performance characteristics, the higher the chances to be able to use these data instead of generating them again during the validation study.

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ICH Q2(R2) / Q14 Training Module 3

Use of Development Data as part of Validation Data

Some examples on usage of development data are following:

- **Selectivity and Specificity:** Using specificity data generated during analytical procedure development as validation evidence.
- **Linearity:** Incorporation of linearity data from the development phase to demonstrate the range of the analytical procedure during validation.
- **Lower Range Limit (DL/QL):** Adapting sensitivity evaluations from development for validation, showing the ability of the analytical procedure to detect and quantify low amounts of analytes.
- **Robustness:** Applying robustness testing data from the analytical procedure development stage to demonstrate analytical procedure reliability under varied conditions.
- **Relative Response Factors:** This evaluation may be performed during validation or development, should use the finalised analytical procedure conditions and should be appropriately documented.
- **System Suitability Testing (SST):** Using SST data from development experiments to confirm system performance during analytical runs.
- **Sample Stability:** Utilising stability data from development studies to demonstrate stability during sample handling and execution of the analytical procedure.

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Lifecycle(ATP, Development, Validation, ECs, Changes) example(s)

- Conclusions

Module 7 shows the following Four case studies

1 Impurity; MEASUREMENT OF STEREOMERS AS SPECIFIC PROCESS RELATED IMPURITIES IN A SMALL MOLECULE DRUG SUBSTANCE

2 Potency; MEASUREMENT OF POTENCY FOR AN ANTI-TNF-ALPHA MONOCLONAL ANTIBODY

3 MAM;MAM(Multi-attribute Method) BY PEPTIDE MAPPING LC-MS

4 NIR; AT-LINE ASSAY OF CORE TABLETS BY MULTIVARIATE ANALYTICAL PROCEDURE IN CONTINUOUS MANUFACTURING OF A DRUG PRODUCT

ATP, Technology Selection, Analytical Procedure Development, Analytical Procedure, Analytical Procedure Validation,

Description of ECs/Reporting categories/Justification,

and Change Management/Bridging Study Change Management/Examples

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ICH Q2(R2) / Q14 Training Module 4

Analytical Target Profile (ATP)

- A prospective summary of the performance characteristics describing the intended purpose and the anticipated performance criteria of an analytical measurement.
- The intended purpose should be sufficiently descriptive for the measurement of the attribute and the use of that result.
- Facilitates the selection of the technology, the procedure design and development as well as the subsequent performance monitoring and continual improvement of the analytical procedure.
- Multiple available analytical techniques may meet the performance requirements.
- Maintained over the lifecycle and can be used as basis for lifecycle management.
  - An ATP could also be retrospectively established.

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Table 1: Analytical Target Profile

Intended Purpose		
Quantitation of the six stereoisomers A - F in Sakuratinib Maleate DS for release testing		
Link to critical quality attribute (CQA) (Stereoisomeric Purity)		
The analytical procedure should allow for the quantitation of the individual stereoisomers A - F and determination of the total sum to verify the CQA Stereoisomeric Purity ≥ 99.0%		
Characteristics of the Reportable Results		
Performance Characteristics	**Acceptance Criteria***	**Rationale**
Accuracy	80 - 120% average recovery of spiked DS with Impurities A - E (specified at NMT 0.1% each) 90 - 110% average recovery of spiked DS with Impurity F (specified at NMT 0.5%)	For example, at a specification level of 0.1%, 20% bias would lead to a variation of the analytical result of 0.02%, which was found acceptable for a release decision. In a similar fashion, values for precision were derived. The recovery criteria for accuracy were set with respect to the reported result and taking into consideration any correction or response factors
Precision	Intermediate Precision relative standard deviation (RSD): Impurities A - E ≤ 15% Impurity F ≤ 10%	
Specificity	Analytical procedure should be able to quantitate impurities A - F in presence of other likely process related substances or DS degradation products with an acceptable bias of not more than 0.02%	Potential interference with quantitation of specified impurities by other regular components in the sample
Reportable Range	Impurities A - E: at least 0.05 - 0.12% Impurity F: at least 0.05 - 0.6%	Reporting threshold to 120% of specification limit

ATP example;
Extracted from module 7 IMPURITY

Link to CQA

Technology is NOT selected yet

For necessary performance characteristics, acceptance criteria are determined

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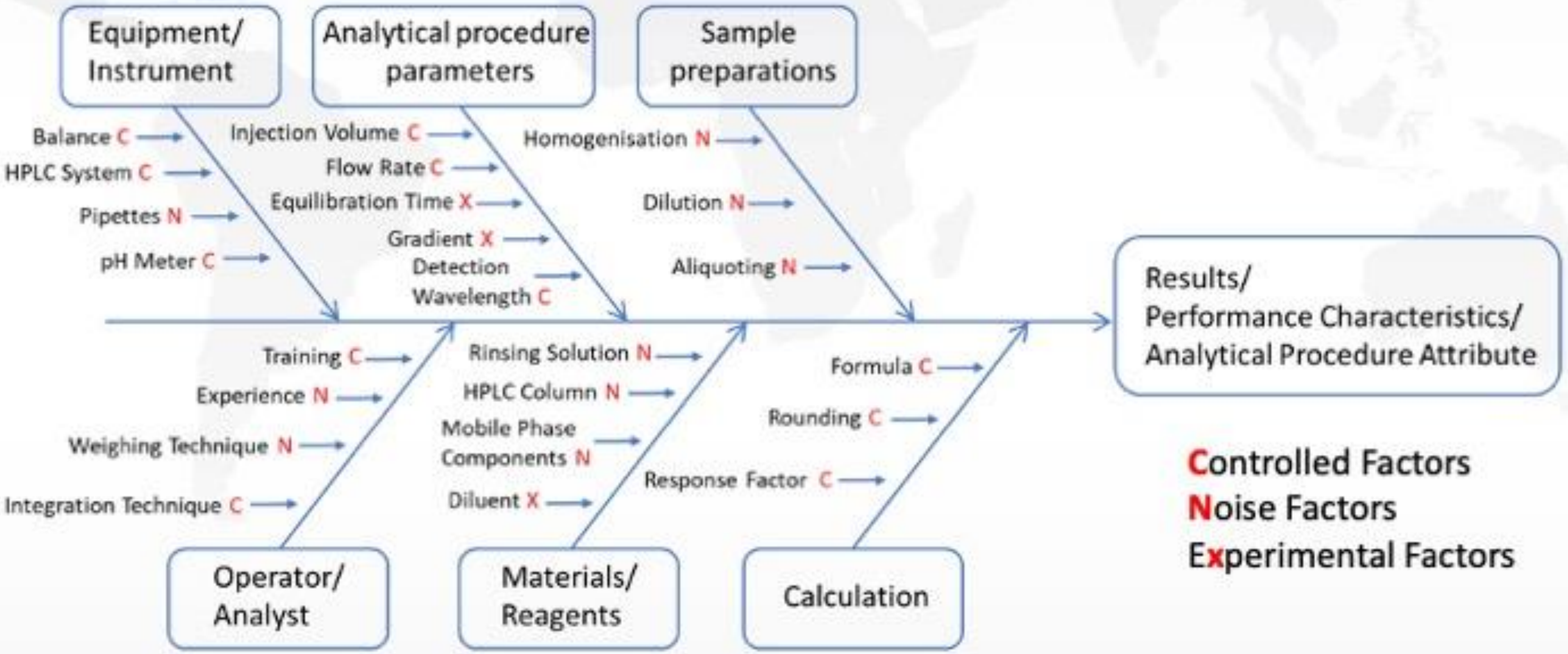
Robustness and Parameter Ranges

This Ishikawa diagram is from module 4.

Case studies in module 7 have specific Ishikawa diagram



Controlled Factors
Noise Factors
Experimental Factors

Risk assessment can inform the selection of parameters to investigate during the robustness study.

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ICH Q2(R2) / Q14 Training Module 5

Risk Reduction for Changes (ICH Q14 Table 1)

ICH Q14 Table 1 illustrates the relationship between risk and prior knowledge when designing studies in support of a proposed change.

Increased risk drives the need for more in-depth studies to support the change.

Lower risk enables confirmatory studies to support the change.

Prior knowledge can be utilised to inform study design.

Reduced prior knowledge requires comprehensive study.

Table 1: Relationship between knowledge (understanding), risk and extent of studies for changes to analytical procedures

Knowledge[1)]	Risk associated with the change: Low	Risk associated with the change: High
High	Prior knowledge or confirmatory study according to a study plan derived from prior knowledge	In depth study according to a study plan derived from prior knowledge
Low	Confirmatory study according to a study plan	In depth study according to a study plan

1) As described in ICH Q10

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Analytical Procedure Control Strategy: Established Conditions (ECs) for Analytical Procedures

- In line with ICH Q12, ECs are legally binding information considered necessary to assure product quality.
  - Any change to ECs necessitates a submission to the regulatory authority.
  - ECs are proposed and justified by the applicant and approved by the regulatory authority.
  - They can be identified using tools in Chapter 2 including risk assessment, prior knowledge, and learnings from uni- and multi-variate experimentation.
- The nature and extent of ECs depends on the development approach, complexity of the analytical procedure and demonstrated understanding.

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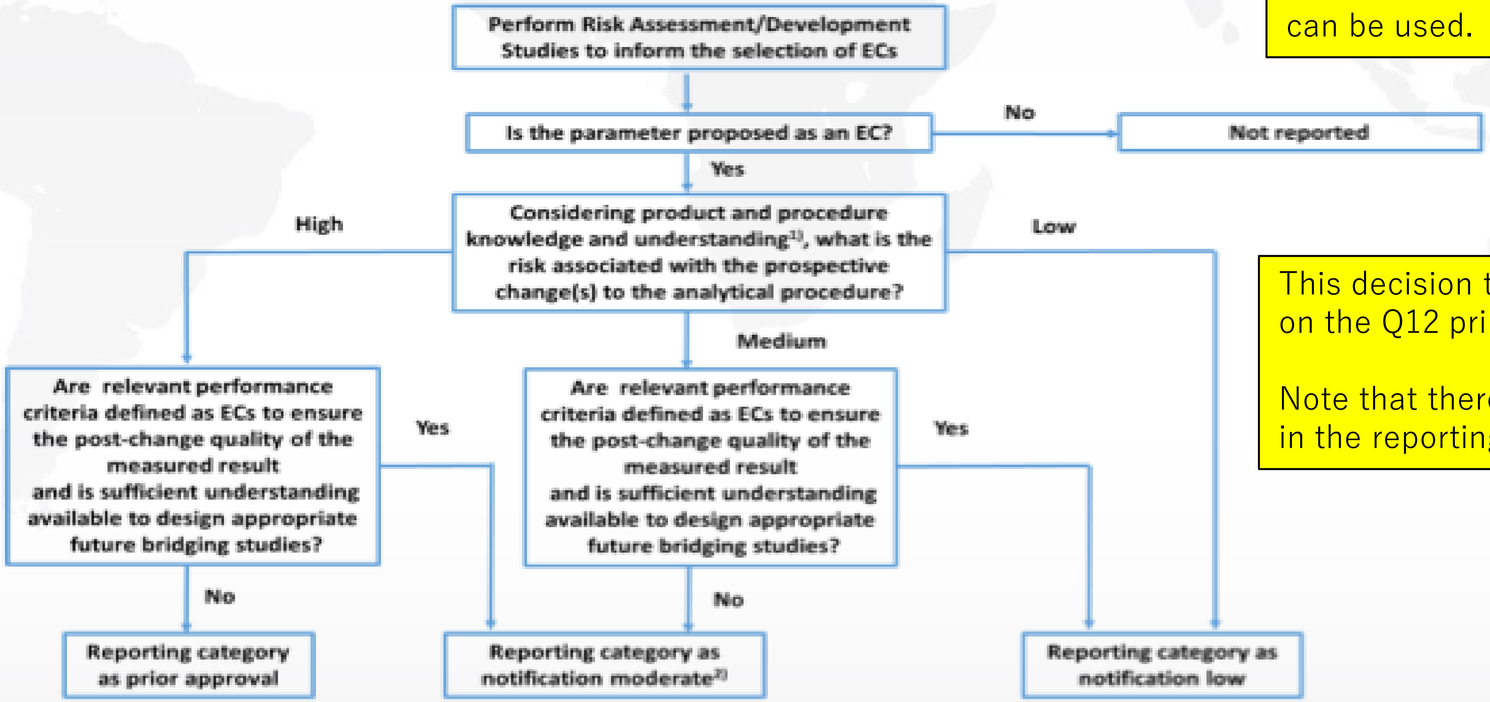
ICH Q2(R2) / Q14 Training Module 5

Lifecycle Management and Post-Approval Changes of Analytical Procedures (ICH Q14 Figure 2)

When ECs are identified with Enhanced Knowledge, the decision tree in this chart can be used.



This decision tree is written based on the Q12 principle.

Note that there are regional differences in the reporting categories

1) Including analytical procedure control strategy.

2) In some cases, moderate risk changes proposed by the company may require prior approval based on health authority feedback.

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Post-approval Change
Technique from chiral HPLC to chiral SFC

Reassessment of the risk of the change with the following points considered
- **Relevance of the test:** High, control of the CQA (quantitation of stereoisomers)
- **Complexity of the test:** well-established technology
- **Extent of the change:** related technologies; prior knowledge of chemistry, process and impurities informs the procedure development

Estimated risk: High

Development approach for chiral SFC procedure
- Enhanced development approach of the same principles as completed for the HPLC procedure was followed
- Risk assessment was conducted to identify the analytical procedure parameters that can impact performance of the procedure
- Modelling and/or multi-variate experiments were performed to explore ranges and interactions between identified analytical procedure parameters
- An analytical procedure control strategy was defined

Re-confirmation of the following points
- **Adherence to criteria for relevant performance characteristics:** Those are defined as ECs
- **Sufficient information or prior knowledge to design appropriate bridging studies:** Yes

Risk assessment result before bridging study execution is in agreement with the submitted risk category.
Overall risk category: Medium

Execution of analytical procedure development
- Procedure parameters for chiral SFC were determined through knowledge of the process and impurities, and enhanced practices for development
- Analytical procedure description (including AP control strategy (SST)) was finalized

Demonstration of analytical procedure performance
- The procedure was validated by a technology specific validation protocol

Risk assessment result before bridging study execution is in agreement with the submitted risk category.
Overall risk category: Medium

Execution of analytical procedure development
- Procedure parameters for chiral SFC were determined through knowledge of the process and impurities, and enhanced practices for development
- Analytical procedure description (including AP control strategy (SST)) was finalized

Demonstration of analytical procedure performance
- The procedure was validated by a technology specific validation protocol
- Through above studies, relevant performance characteristics and the analytical procedure attributes were evaluated and confirmed
- Execution of bridging study (ICH Q14 Table 2)

Conclusions
The impact of the change was determined based on the bridging study result
- **Impact on the test performance:** The relevant performance characteristics and the analytical procedure attributes met their criteria
- Bridging study results met all acceptance criteria

Regulatory reporting
Reported according to the pre-agreed reporting category in registration as notification moderate and submitted suitable documents.

From module 7, impurity.
Change #2; HPLC to SFC

Outline of This Presentation

- Overview of the two guidelines

- Structure of the training materials and read suggestions

- Key points with examples/cases

Validation study vs. Validation test *(Validation strategy, Development data, MODR, Platform)*

Lifecycle(ATP, Development, Validation, ECs, Changes) example(s)

- **Conclusions**

Considerations

- The ICH Q14 and ICH Q2(R2) guidelines should be applied in conjunction with other existing and prospective ICH "Q" guidelines, including ICH 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.

Use Q2 and Q14 together.
And with others, Q8-Q13.

The enhanced approach yields
comprehensive knowledge

Conclusions

- The ICH Q14 and ICH Q2(R2) guidelines establish harmonised scientific and technical principles for analytical procedures 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 modernised to include newer technologies (e.g., for biological products or multivariate analytical procedures).

Thank you
for the attention!

Q2/Q14 EWG Group Photo in Vancouver, June 2023