Global Expertise
Trusted Standards
Improved Health

U.S. Pharmacopeial Convention

Lifecycle Management Concepts to Analytical Procedures

Horacio Pappa, Ph.D.
Director - General Chapters
U.S. Pharmacopeia

USP Definitions

- <1225> Validation of Compendial Procedures
  Validation will be required when
  - an analytical procedure is used to test a non-official article.
  - an official article is tested using an alternative procedure (see *USP General Notices 6.30*).

- <1226> Verification of Compendial Procedures
  Verification will be required the first time an official article is tested using a USP procedure.

- <1224> Transfer of Analytical Procedures
  Transfer will applies when a non-compendial procedure is moved from one lab to another.

Validation – USP Definition

"Validation of an analytical procedure is the process by which it is established, by laboratory studies, that the performance characteristics of the procedure meet the requirements for the intended analytical applications."

<1225> Validation of Pharmacopeial Procedures

Performance Characteristics	Category I	Category II		Category III	Category IV
		Qty	Limit		
Accuracy	**Yes**	**Yes**	*	*	**No**
Precision	**Yes**	**Yes**	**No**	**Yes**	**No**
Specificity	**Yes**	**Yes**	**Yes**	*	**Yes**
LOD	**No**	**No**	**Yes**	*	**No**
LOQ	**No**	**Yes**	**No**	*	**No**
Linearity	**Yes**	**Yes**	**No**	*	**No**
Range	**Yes**	**Yes**	*	*	**No**

* May be required depending on the type of test.

Allowance for alternative procedures in USP

USP General Notices:

6.30

Alternative methods and/or procedures may be used if they provide advantages in terms of accuracy, sensitivity, precision, selectivity, or adaptability to automation or computerized data reduction, or in other special circumstances. Such alternative procedures and methods shall be validated as described in the general chapter Validation of Compendial Procedures <1225 > and **must be shown to give equivalent or better results.**

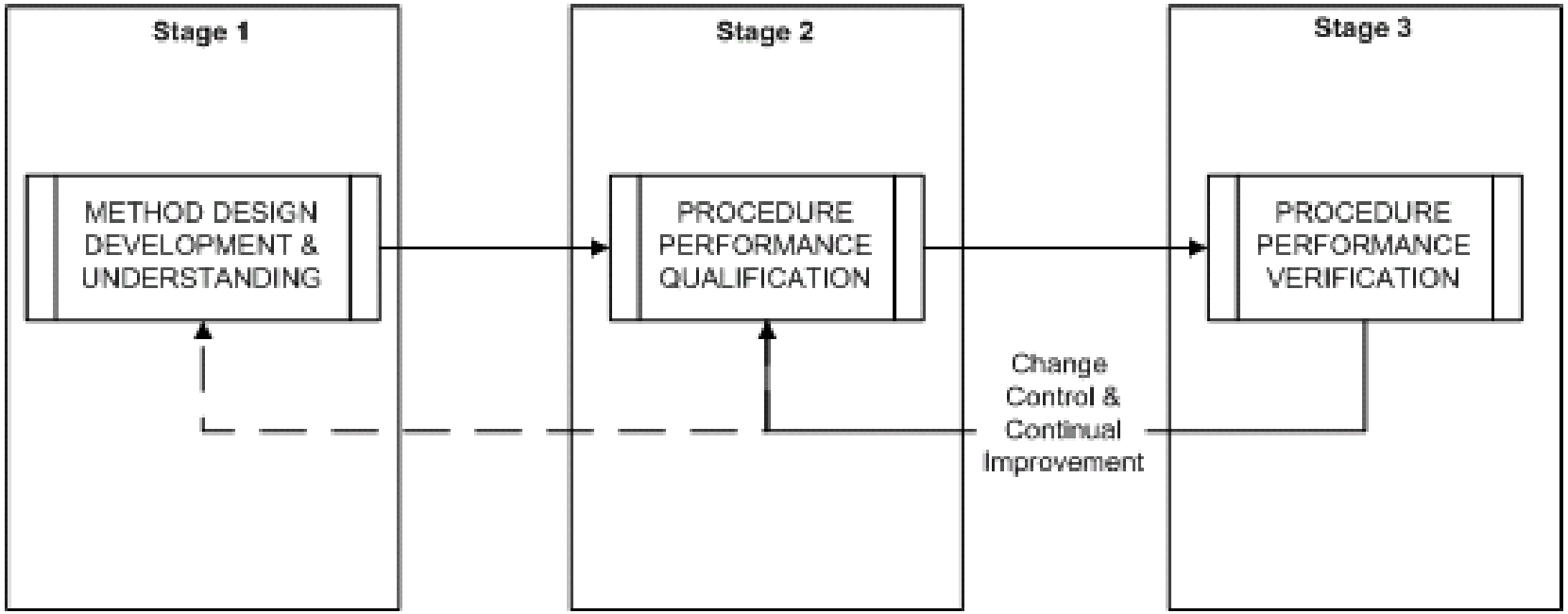
One step forward

- ICH Q10 Pharmaceutical Quality Systems
- ICH Q9 Quality Risk Management
- ICH Q8 Pharmaceutical Development

Lifecycle Management of Analytical Procedures

- Adaptation of the lifecycle concept [ICH Q8] and of modern concepts for process validation to analytical procedures
  - to holistically align analytical procedure variability with the requirements of the product to be tested
  - to demonstrate that the analytical procedure meets the predefined criteria over the whole lifecycle
  - to facilitate continual improvement
- Stimuli article is published in PF 39(5), Sep - Oct 2013

Lifecycle approach for analytical procedures validation



Lifecycle Approach to Validation of Analytical Procedures with Related Statistical Tools Workshop

December 8-9, 2014 · USP Headquarters, Rockville, Maryland USA

Co-sponsored by

aaps American Association of Pharmaceutical Scientists

IQ International Consortium for Innovation & Quality in Pharmaceutical Development

Topics to Include:

- QbD, the Product Lifecycle model applied to analytical procedures
- Risk analysis/control strategy throughout the lifecycle
- How to establish an analytical target profile
- Measurement uncertainty: what it is, how it is used in the analytical target profile, and how to estimate it
- Statistical tools to support the development, qualification, and verification of the analytical procedure throughout the lifecycle
- Current regulatory perspective
- Case studies and examples

<1220> Prospectus

General Chapter Prospectus: <1220> The Analytical Procedure Lifecycle

Type of Posting	General Announcement
Posting Date	24–Jun–2016
Expert Committee	General Chapters—Chemical Analysis

Input Deadline: 29–Jul–2016

Current or Proposed GC Title: <1220> The Analytical Procedure Lifecycle

Suggested audience: Drug product manufacturers, dietary supplement manufacturers, testing organizations, and drug product related regulatory agencies.

Estimated proposal *PF*: 43 (1) [Jan.–Feb. 2017]

Background and objective(s): An analytical procedure must be shown to be fit for its intended purpose. It is useful to consider the entire lifecycle of an analytical procedure when approaching development of the procedure, i.e. its design, development, qualification, and continued verification. The current concepts of validation, verification, and transfer of procedures address portions of the lifecycle but do not consider them holistically. This General Chapter intends to more fully address the entire procedure lifecycle and define concepts which may be useful. This approach is consistent with the concepts of Quality by Design (QbD) as described in ICH Q8 (R2), 9, 10, and 11.

Preliminary outline:

- THE LIFECYCLE APPROACH
  - Analytical target profile
- STAGE 1: PROCEDURE DESIGN, DEVELOPMENT, AND UNDERSTANDING
  - Procedure design and development
  - Procedure understanding
  - Preparing for qualification
- STAGE 2—PROCEDURE PERFORMANCE QUALIFICATION
- STAGE 3—IMPLEMENTATION AND CONTINUED PROCEDURE PERFORMANCE VERIFICATION
  - Routine monitoring
  - Analytical control strategy
  - Knowledge management
  - Change control

<1225> Proposal in PF 42(2)

Add the following:

LIFE CYCLE MANAGEMENT OF ANALYTICAL PROCEDURES

Once a compendial procedure is successfully validated (or verified) and implemented, the procedure should be monitored during the routine use to continually assure that the procedure remains fit for its intended purpose. Trend analysis on performance should be carried out in order to provide documented evidence that the procedure performs to the required standard and to evaluate the need to optimize and revalidate all or a part of the analytical procedure. If an analytical procedure can only meet the established system suitability requirements with repeated adjustments to the operating conditions stated in the analytical procedure, the analytical procedure should be reevaluated, amended, and revalidated, as appropriate. Over the commercial life of a product, new information and risk assessments (e.g., awareness of a new impurity) may necessitate the development and validation of a new or an alternative analytical procedure. New technologies used for testing may allow for greater understanding and/or confidence when testing (or assessing) product quality. Therefore, the appropriateness of analytical procedures should also be periodically evaluated, and new or alternative validated procedures may be considered. **1S (*USP40*)**

Val & Ver EP's activities

- PF 42(2) Fitness for Use: Decision Rules and Target Measurement Uncertainty [PF42(2)]

- Two more papers to be published in PF 42(5)
  - Analytical target profile (ATP): Structure and application throughout the analytical lifecycle
  - Analytical control strategy

- Second workshop to be held in Europe in November, 2016

- PF 43(1): Proposed New USP General Chapter: The Analytical Procedure Lifecycle <1220> .

PF 43(1): Stim article: The Analytical Procedure Lifecycle <1220>

- The EC considers this is an evolving concept
- No changes in <1224>, <1225>, and <1226>.
- Chemical Analysis Expert Committee is seeking input regarding the following questions:
  - Would a general chapter on the lifecycle approach be valuable?
  - Is the information presented herein sufficient for implementation of aQbD approach?
  - Would incorporation of references to statistical tools be valuable?
  - Can you provide input or approaches that would improve this proposed general chapter?

Thank You