ICHQ14 and USP Chapter <1220>: Historical perspective and the path forward in Analytical QbD

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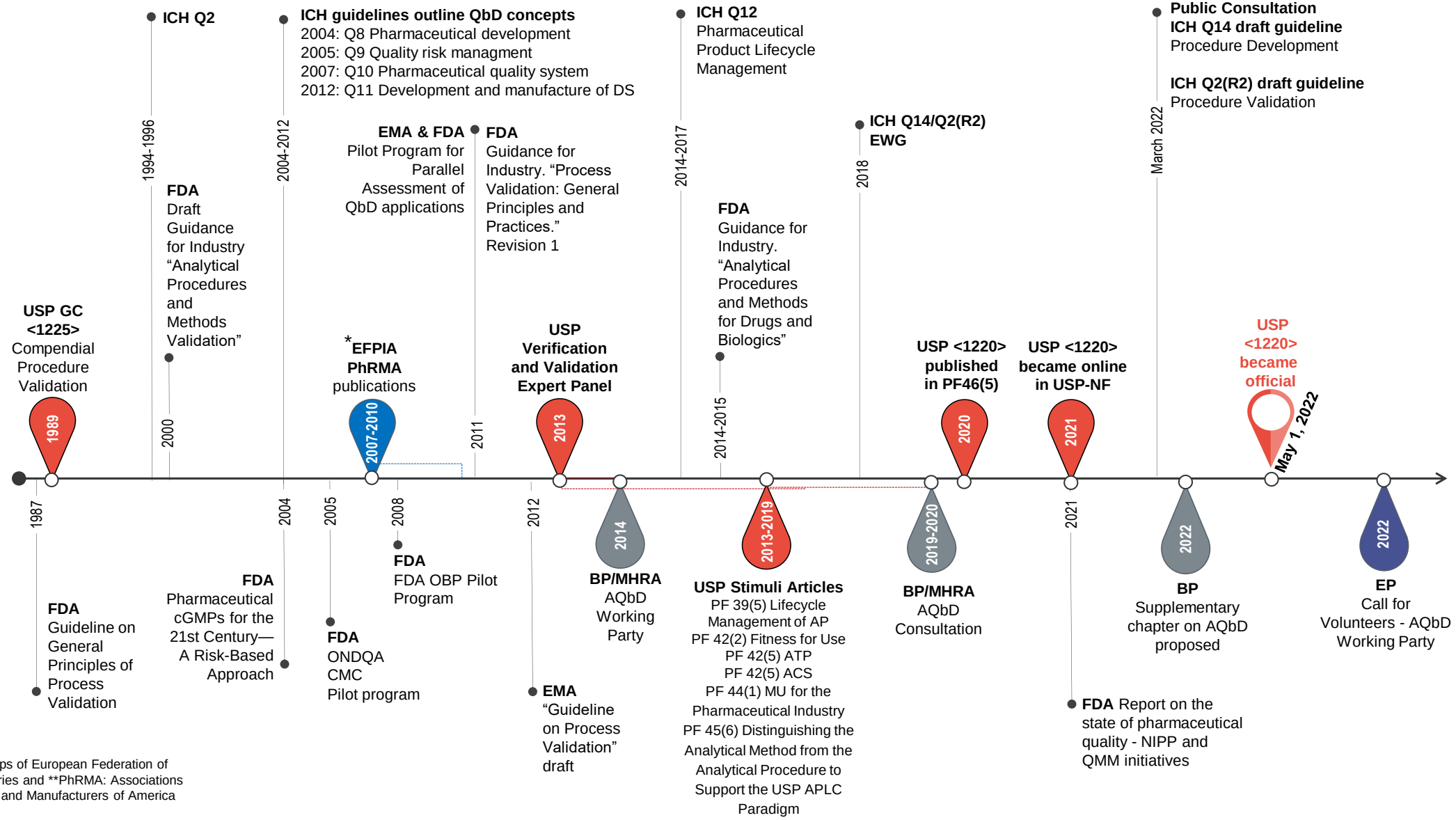
Empowering a healthy tomorrow

Evolution of QbD and AQbD



*EFPIA: joint working groups of European Federation of the Pharmaceutical Industries and **PhRMA: Associations Pharmaceutical Industries and Manufacturers of America

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Analytical Procedure Life Cycle

Concept

- “Framework for analytical procedures that holistically incorporates all the events that take place over the procedure life cycle that are designed to demonstrate that a procedure is, and remains, fit for the intended purpose”

AQbD:

"Systematic approach that begins with predefined objectives (ATP) and emphasizes analytical procedure understanding and control based on sound science and quality risk management.”

- Alignment with ICH: Q8 (Pharmaceutical development); Q9 (QRM); Q10 (PQS); Q12 (Life Cycle Management)
- Validation, or demonstration that a procedure is suitable for the intended purpose, takes place during the entire procedure life cycle, beginning during the initial procedure design activities and extending through routine use. These activities include the formal procedure validation, verification, and transfer of procedures, as well as establishing and ensuring adherence to an appropriate set of procedure controls and system suitability requirements.
- The procedure life cycle approach is applicable to all types of analytical procedures, and the extent of effort should be consistent with the complexity of the procedure and the criticality of the quality attribute to be measured.

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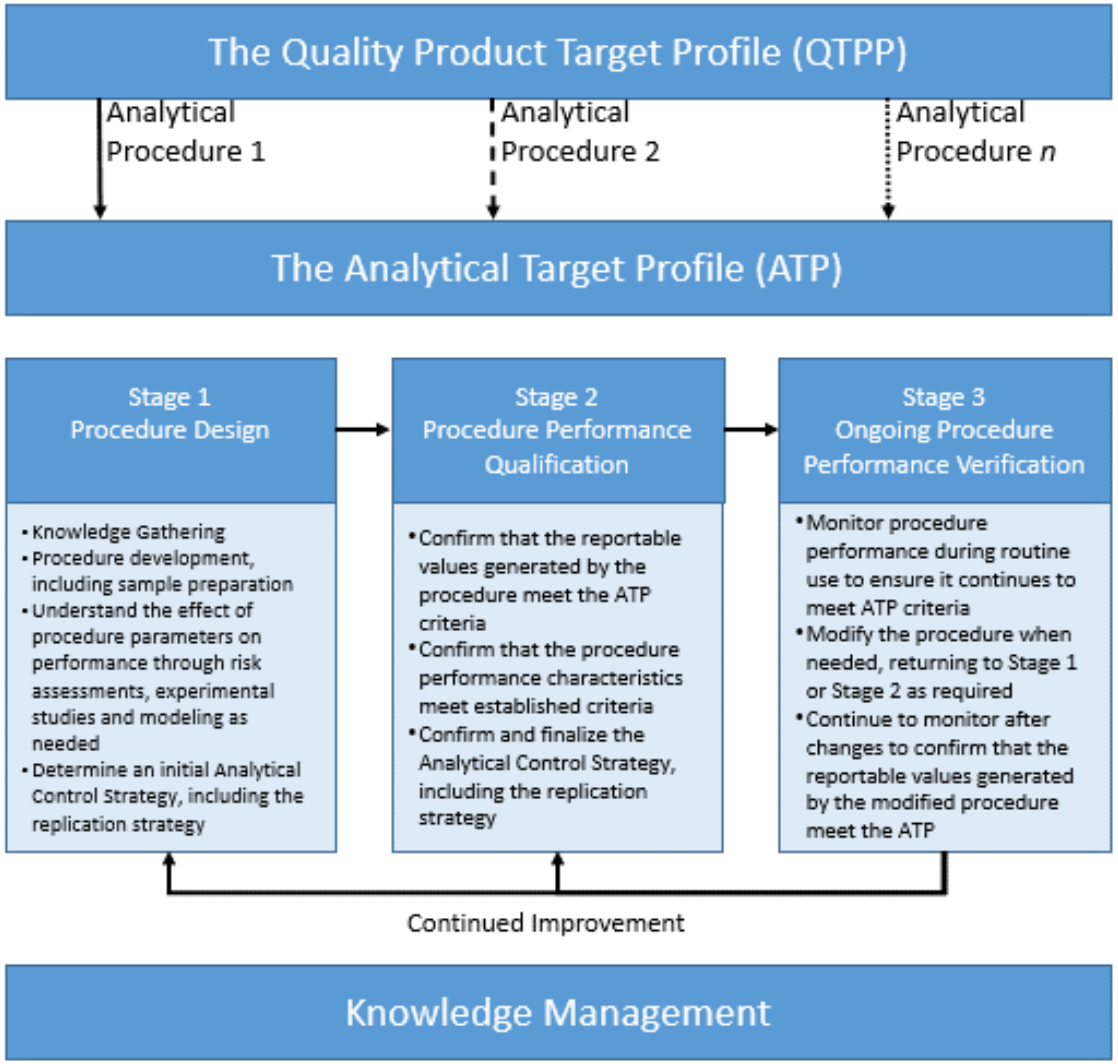
Analytical Procedure Life Cycle



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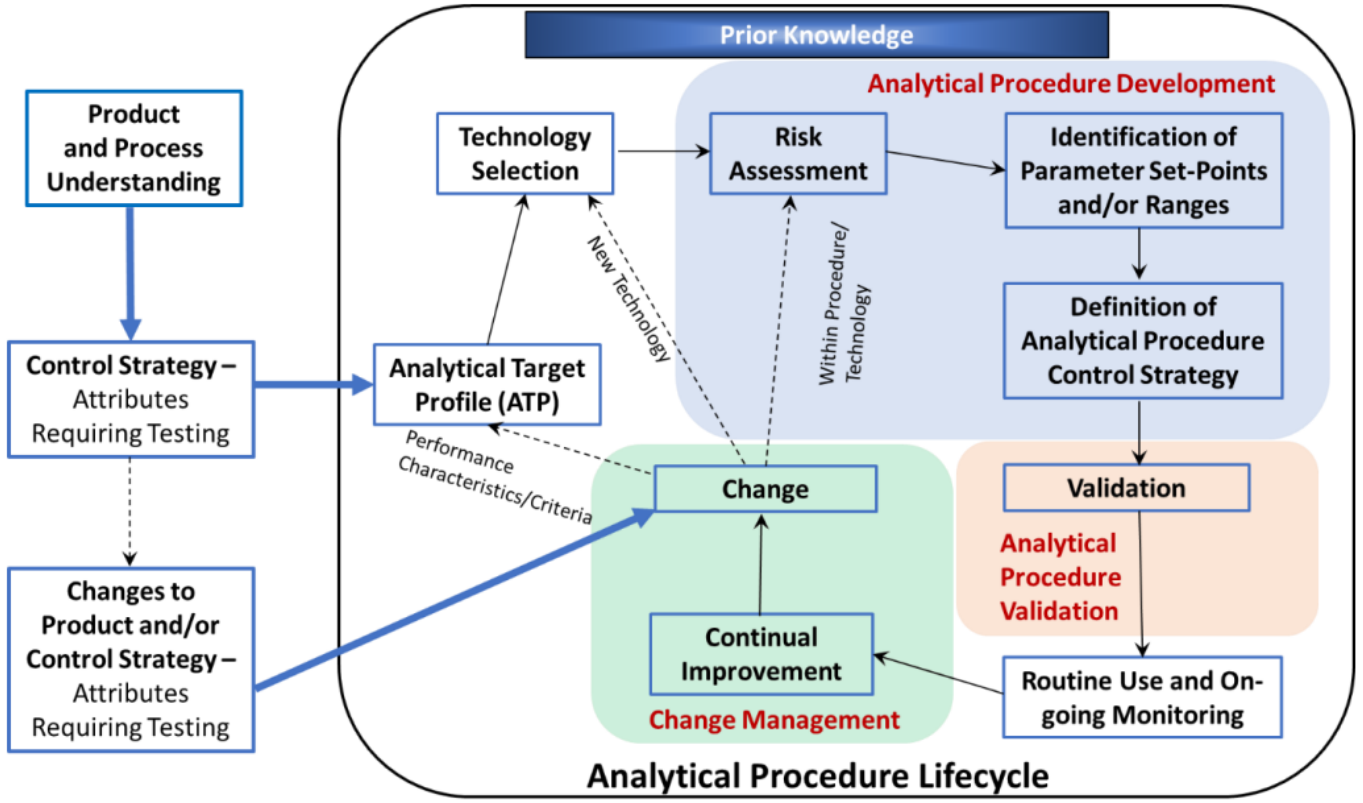

ICH Q14

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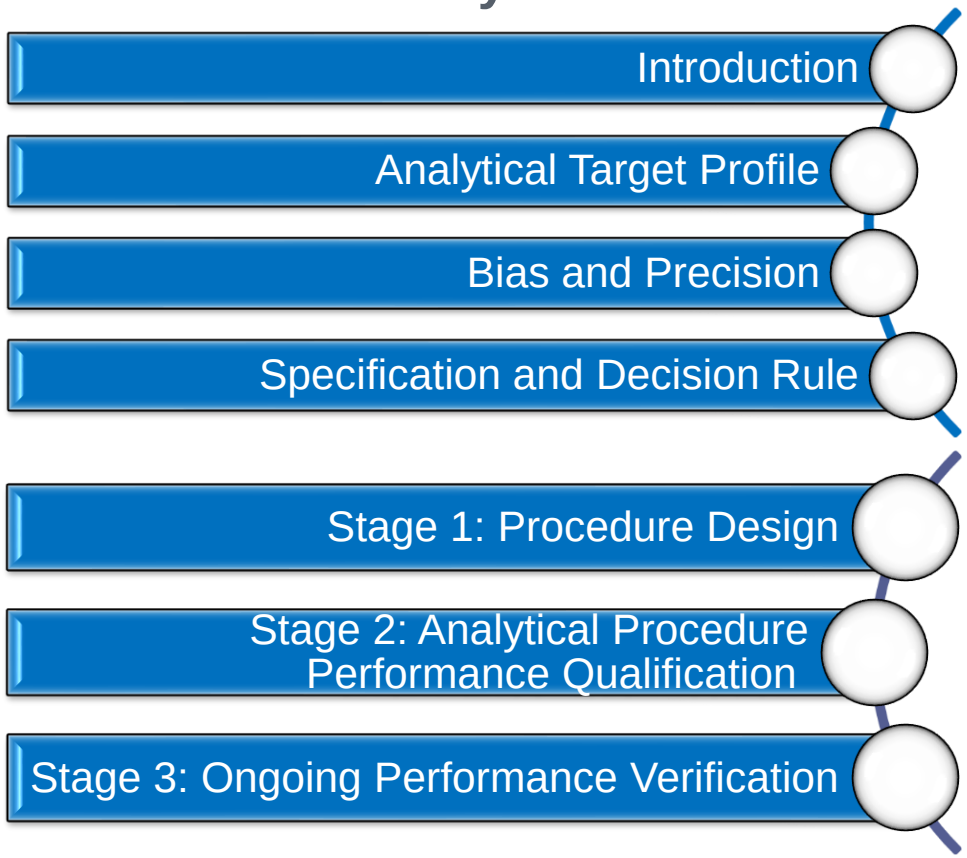
USP GC <1220> & ICH Q14

Q14 Analytical Procedure Development

<1220> Analytical Procedures Life Cycle



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Analytical Target Profile (ATP)

- USP <1220>: ATP is a prospective description of the desired performance for an analytical procedure that is used to measure a quality attribute.
- ICH Q14: An ATP consists of a description of the intended purpose, appropriate details on the product attributes to be measured and relevant performance characteristics with associated performance criteria.
- It drives the selection of the analytical technology

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Knowledge management

- Relevant prior knowledge can assist with the selection of the technology and development activities. It may include:
  - Physical and chemical properties of the analytes,
  - Information in the scientific literature,
  - Existing procedures for the analysis of the similar material attributes.
  - The availability of any relevant analytical technology and/or platform analytical procedures (applicable to materials of similar type)
- Any other relevant information linked to the operational requirements, such as instrumentation setup and sample preparation
- As additional knowledge is obtained, it should be actively managed throughout the product lifecycle

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Quality Risk management (QRM)

ICH Q14

- Risk assessment is typically performed early in analytical procedure development and is repeated as more information becomes available. Risk assessment can be formal or informal and can be supported by prior knowledge
- Can be used to establish the procedure control strategy
- Risk assessment tools as described in ICH Q9

USP <1220>

- QRM activities can be applied to assess the proposed procedure conditions and identify appropriate controls on the analytical procedure parameters (Ishikawa diagrams, heat maps, etc.)
- QRM activities can be applied during procedure development either formally or informally and major sources of bias and variability can be identified, reduced or even eliminated by ensuring the appropriate technology and procedure conditions.
- QRM tools like Ishikawa diagram and heat maps

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ANALYTICAL PROCEDURE PERFORMANCE QUALIFICATION (<1220>)

- Occurs in Stage 2 of the life cycle and evaluates the procedure to determine if it is capable of consistently generating a reportable value that meets the defined ATP and if it is capable of consistently generating a reportable value that meets the defined ATP and is suitable for its intended purpose in the laboratory
- APPQ encompasses all of the analytical procedure activities as qualification, verification, validation, and transfer described in other literature and guidances.
- **At the end of stage 2 the replication strategy is confirmed, and it is confirmed that the performance of the procedure meets the ATP and other criteria.**

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Analytical Procedure Validation (ICH Q14)

- The goal of development is to obtain an analytical procedure fit for its intended purpose: to measure an attribute or attributes of the analyzed material with the needed specificity/selectivity, accuracy and/or precision over the reportable range.
- In general, data gained during the development studies (e.g., robustness data from a design of experiments) can be used as validation data for the related analytical procedure performance characteristics and does not necessarily need to be repeated.
- References to ICH Q2

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Continued Performance Verification vs Ongoing monitoring

It involves monitoring the analytical procedure during use and confirming that the ATP criteria are still being met.

- Routine Monitoring Effective monitoring of an analytical procedure provides ongoing confidence that the reportable values generated are fit for purpose.
- Analytical Control Attributes example SST attributes such as system precision, signal-to-noise ratio, or peak symmetry
- Control Charts recommended practice for monitoring of method performance attributes and control sample results
- Changes to an Analytical Procedure changes should be risk assessed for their impact to determine the appropriate activities required. In addition, appropriate change management approaches and documentation should be used when make changes to a procedure.

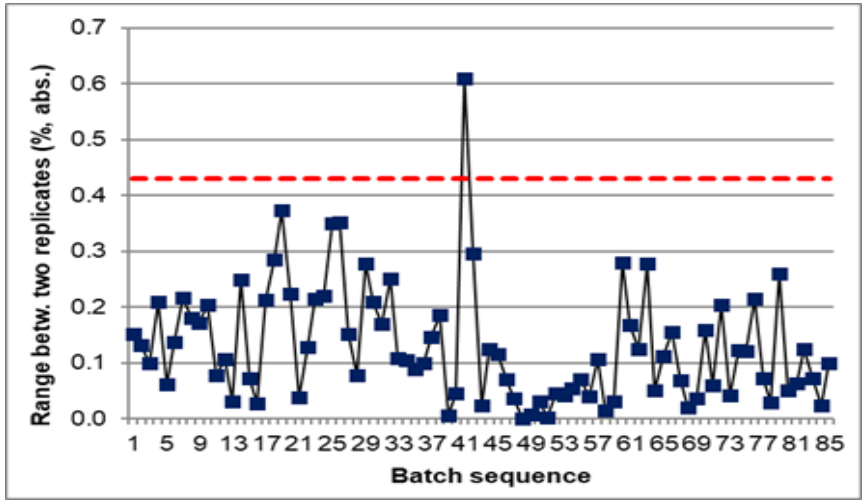

Figure 8. Example of a control chart for an API titration content range from two replicate determinations.

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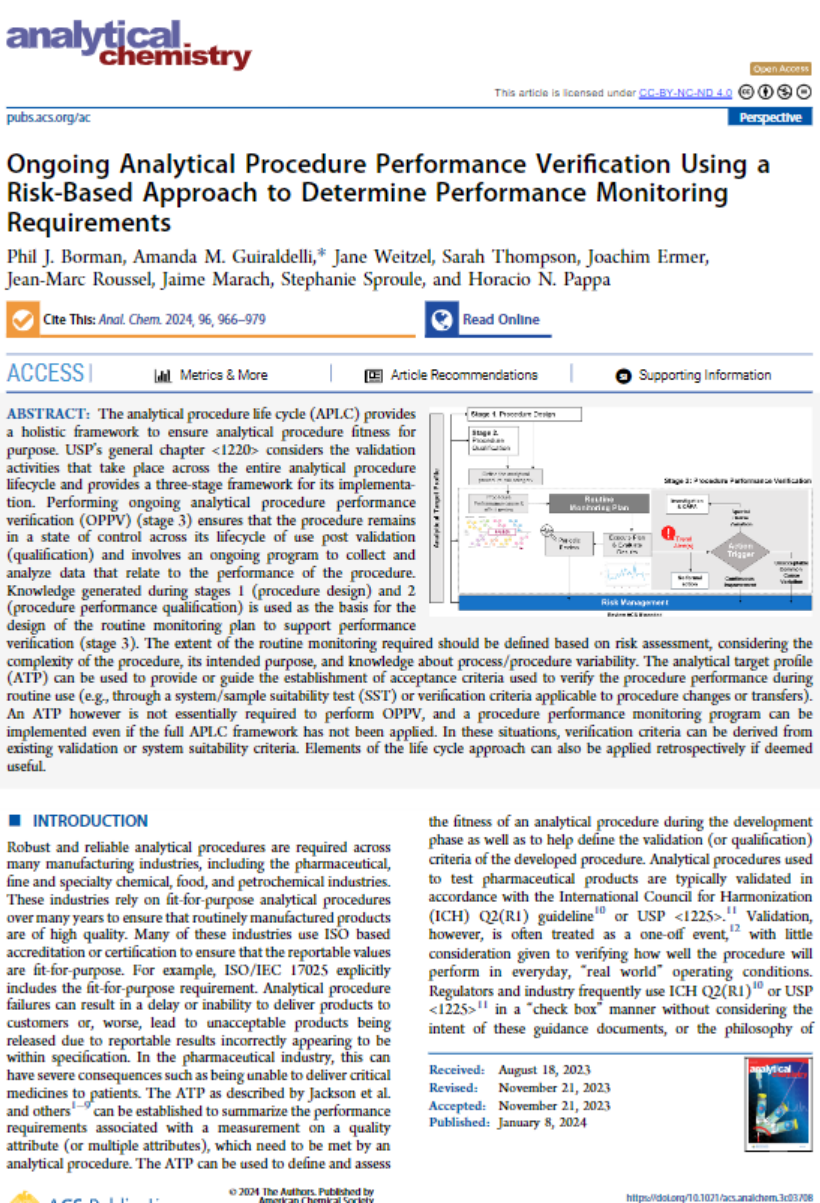
Ongoing Procedure Performance Verification (Stage 3)



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Perspective

Ongoing Analytical Procedure Performance Verification Using a Risk-Based Approach to Determine Performance Monitoring Requirements

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Cite This: *Anal. Chem.* 2024, 96, 966–979

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ABSTRACT: The analytical procedure life cycle (APLC) provides a holistic framework to ensure analytical procedure fitness for purpose. USP's general chapter <1220> considers the validation activities that take place across the entire analytical procedure lifecycle and provides a three-stage framework for its implementation. Performing ongoing analytical procedure performance verification (OPPV) (stage 3) ensures that the procedure remains in a state of control across its lifecycle of use post validation (qualification) and involves an ongoing program to collect and analyze data that relate to the performance of the procedure. Knowledge generated during stages 1 (procedure design) and 2 (procedure performance qualification) is used as the basis for the design of the routine monitoring plan to support performance verification (stage 3). The extent of the routine monitoring required should be defined based on risk assessment, considering the complexity of the procedure, its intended purpose, and knowledge about process/procedure variability. The analytical target profile (ATP) can be used to provide or guide the establishment of acceptance criteria used to verify the procedure performance during routine use (e.g., through a system/sample suitability test (SST) or verification criteria applicable to procedure changes or transfers). An ATP however is not essentially required to perform OPPV, and a procedure performance monitoring program can be implemented even if the full APLC framework has not been applied. In these situations, verification criteria can be derived from existing validation or system suitability criteria. Elements of the life cycle approach can also be applied retrospectively if deemed useful.

INTRODUCTION

Robust and reliable analytical procedures are required across many manufacturing industries, including the pharmaceutical, fine and specialty chemical, food, and petrochemical industries. These industries rely on fit-for-purpose analytical procedures over many years to ensure that routinely manufactured products are of high quality. Many of these industries use ISO based accreditation or certification to ensure that the reportable values are fit-for-purpose. For example, ISO/IEC 17025 explicitly includes the fit-for-purpose requirement. Analytical procedure failures can result in a delay or inability to deliver products to customers or, worse, lead to unacceptable products being released due to reportable results incorrectly appearing to be within specification. In the pharmaceutical industry, this can have severe consequences such as being unable to deliver critical medicines to patients. The ATP as described by Jackson et al. and others[1−9] can be established to summarize the performance requirements associated with a measurement on a quality attribute (or multiple attributes), which need to be met by an analytical procedure. The ATP can be used to define and assess the fitness of an analytical procedure during the development phase as well as to help define the validation (or qualification) criteria of the developed procedure. Analytical procedures used to test pharmaceutical products are typically validated in accordance with the International Council for Harmonization (ICH) Q2(R1) guideline[10] or USP <1225>.[11] Validation, however, is often treated as a one-off event,[12] with little consideration given to verifying how well the procedure will perform in everyday, "real world" operating conditions. Regulators and industry frequently use ICH Q2(R1)[10] or USP <1225>[11] in a "check box" manner without considering the intent of these guidance documents, or the philosophy of

Received: August 18, 2023
Revised: November 21, 2023
Accepted: November 21, 2023
Published: January 8, 2024

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https://doi.org/10.1021/acs.analchem.3c03708

OPEN ACCESS ARTICLES:

- *Ongoing Analytical Procedure Performance Verification - Stage 3 of USP <1220>.* P. Borman, A. Guiraldelli, J. Weitzel, S. Thompson, J. Ermer, S Sproule, J. Roussel, J. Marach, & H. Pappa. (2023). ***Pharm Tech*, March 2023, Volume 47, 40–44**

- *Ongoing Analytical Procedure Performance Verification Using a Risk-based Approach to Determine Performance Monitoring Requirements.* P. Borman, A. Guiraldelli, J. Weitzel, S. Thompson, J. Ermer, S Sproule, J. Roussel, J. Marach, & H. Pappa. ***Anal. Chem.* 2024, 96, 3, 966–979**

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Final comments

- Both documents formalize the use of the ATP concept to establish a clear description of fit for purpose.
- Traditional or enhanced approaches during Analytical Procedure Life Cycle can be applied.
- Knowledge and quality risk management (QRM) are presented as key enablers of the enhanced approach.
- The use of multivariate experiments, PARs, or MODR to support change managment through the Lifecycle is encourage.
- Both documents emphasizes the importance of establishing APCS and recommends ongoing monitoring to look for any trends.
- Q14 brings a section dedicated to development of multivariate AP and real-time release testing (RTRT).
- Q14 includes a section on submission that harmonize the information to be presented to regulators.

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Thank You