

WCBP Workshop

From Batch Data to
Patient Needs:
Rethinking
Specifications in ICH Q6

Workshop structure

1. Short introduction to the topic

2. Discussion with Audience on experience related to specification justification

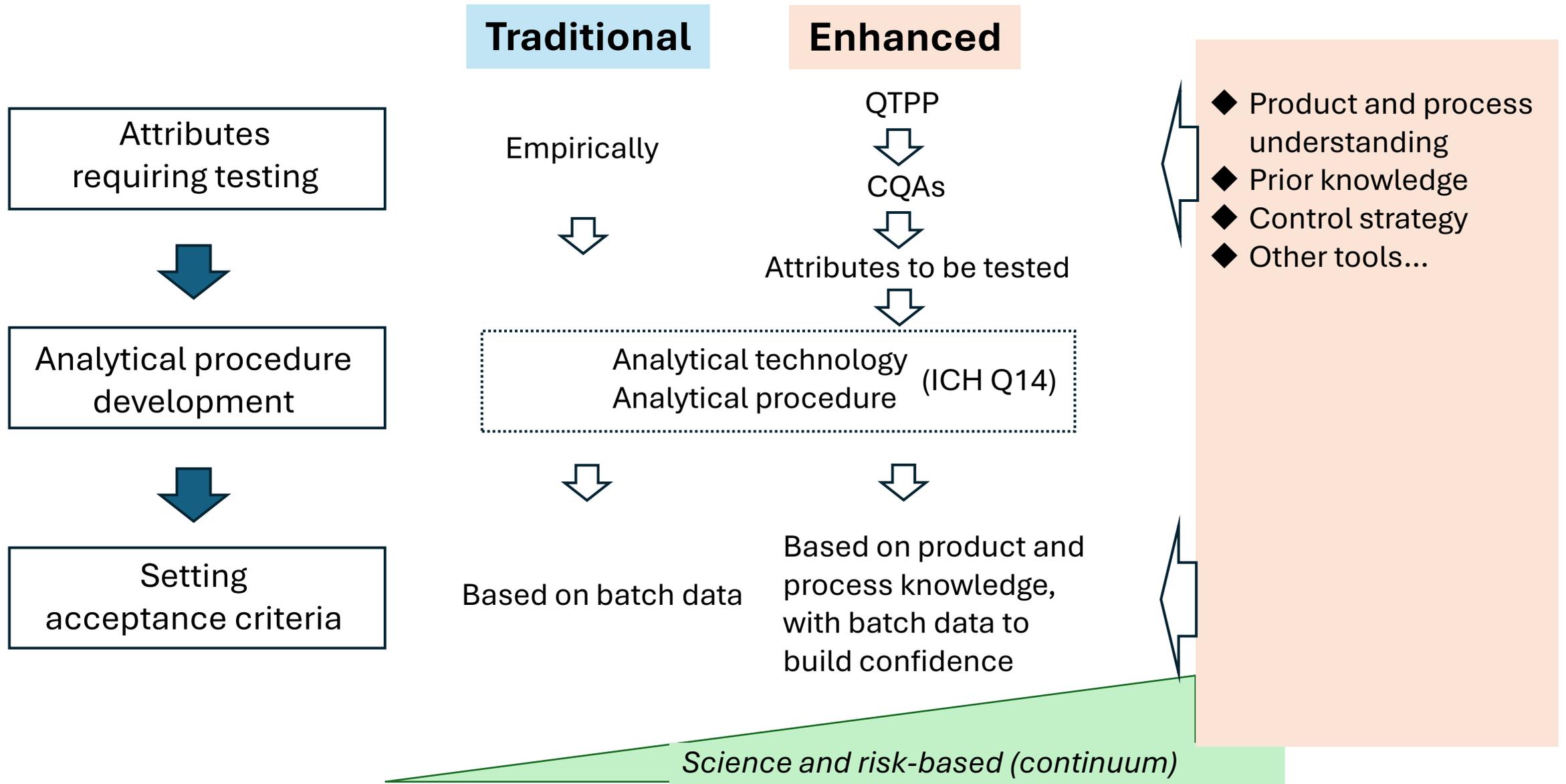
3. Wrap-up

Modernisation of Q6 guidelines

https://database.ich.org/sites/default/files/ICH_Q6%28R1%29_Final_ConceptPaper_2024_0625.pdf

- The modern regulatory perspective emphasizes a science and risk-based approach for establishing specifications.
- Therefore, updating ICH Q6A and Q6B introduces an opportunity to set specification based on holistic approaches that would include e.g.:
 - ✓ Appropriate use of **prior knowledge**;
 - ✓ Appropriate use of pharmaceutical **development data**;
 - ✓ **Prospective** process and product (CQA and CPP) understanding;
 - ✓ Considerations of the overall **control strategy**;
 - ✓ Appropriate use of **modelling tools** and statistical evaluations;
 - ✓ **Non-clinical and clinical relevance**;
 - ✓ Impact to the **safety and efficacy** of the drug product.

Approaches for setting specifications



Questions for discussion

- Do you have any example of traditional or enhanced approach (or a combination of both) based on your experience ?
- What are the anticipated challenges and opportunities with enhanced approach implementation?
- Any specific consideration for recent modalities (e.g., ADCs, CGTs,...)?

Industry & Regulators' perspectives welcome

Examples (back-up)

Approaches for acceptance criteria justification at release and stability

- Integration of traditional & enhanced approach
- Quality attribute selection for specifications (related substance vs related impurities)

Extract from presentation of K. Kearns, “Case Studies for Patient-Centric Specification Setting for a Therapeutic Protein”

CMC Strategy Forum North America 2025, 27 January 2025

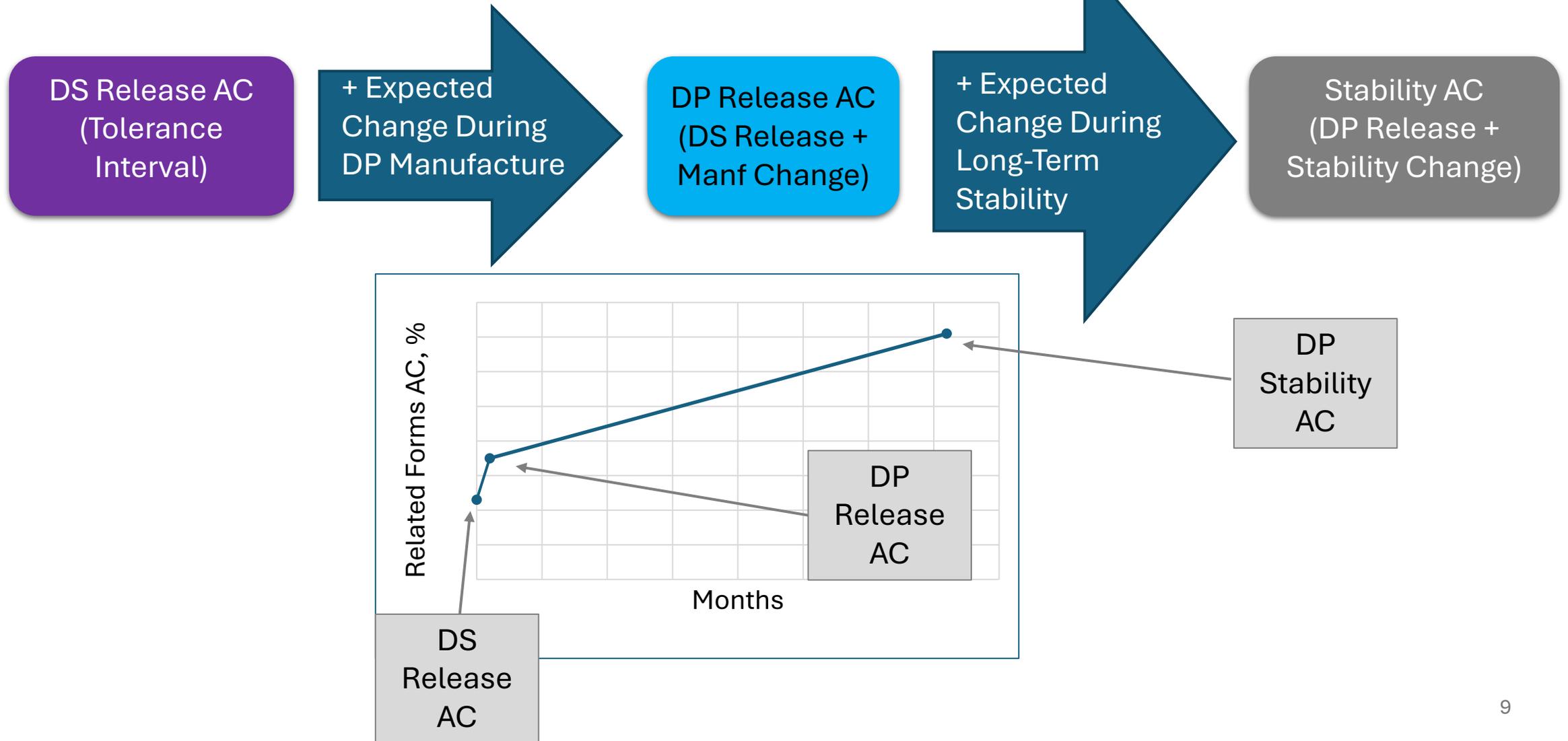
Example 2 – Related Forms (RP-HPLC) Acceptance Criteria

- Multi-use autoinjector with weekly dosing at home for a maximum of 28 days
- Temperature-sensitive attribute

Quality Attribute	Justification	Proposed Strategy	Approved Strategy	Post-Marketing Update Strategy
Related Forms (Deamidation, Oxidation, Isomerization, etc.)	Structure / function studies, literature supporting safety and efficacy at high levels, and clinical batch data	<p>DP Release: DS Tolerance Interval + Change During DP Manufacture</p> <p>DP Stability: DP Release + Change During Stability</p>	<p>DP Release: DS 3x SD + Change During DP Manufacture</p> <p>DP Long-Term Stability: DP Release + Change During Stability</p> <p>DP In-Use Stability: DP Long-Term Stability + Projected Change During In-Use Stability</p>	<p>DP Release: DS 3x SD + Change During DP Manufacture</p> <p>DP Long-Term Stability: DP Release + Change During Stability</p> <p>DP In-Use Stability: DP Long-Term Stability + Change During In-Use Stability</p>

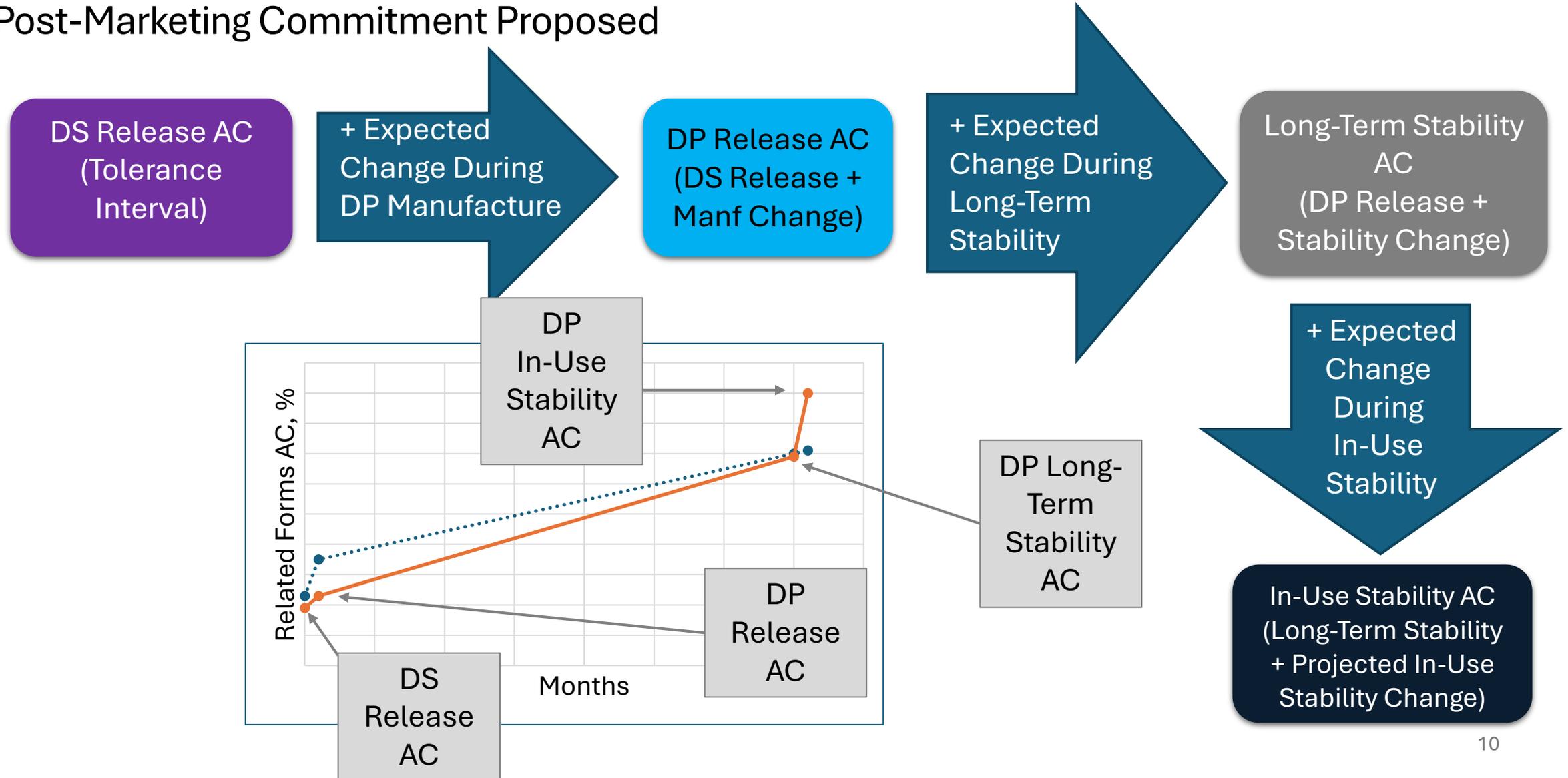
Example 2: Related Forms (RP-HPLC) - Initial Proposal

Based on Release and Long-Term Stability Data Only



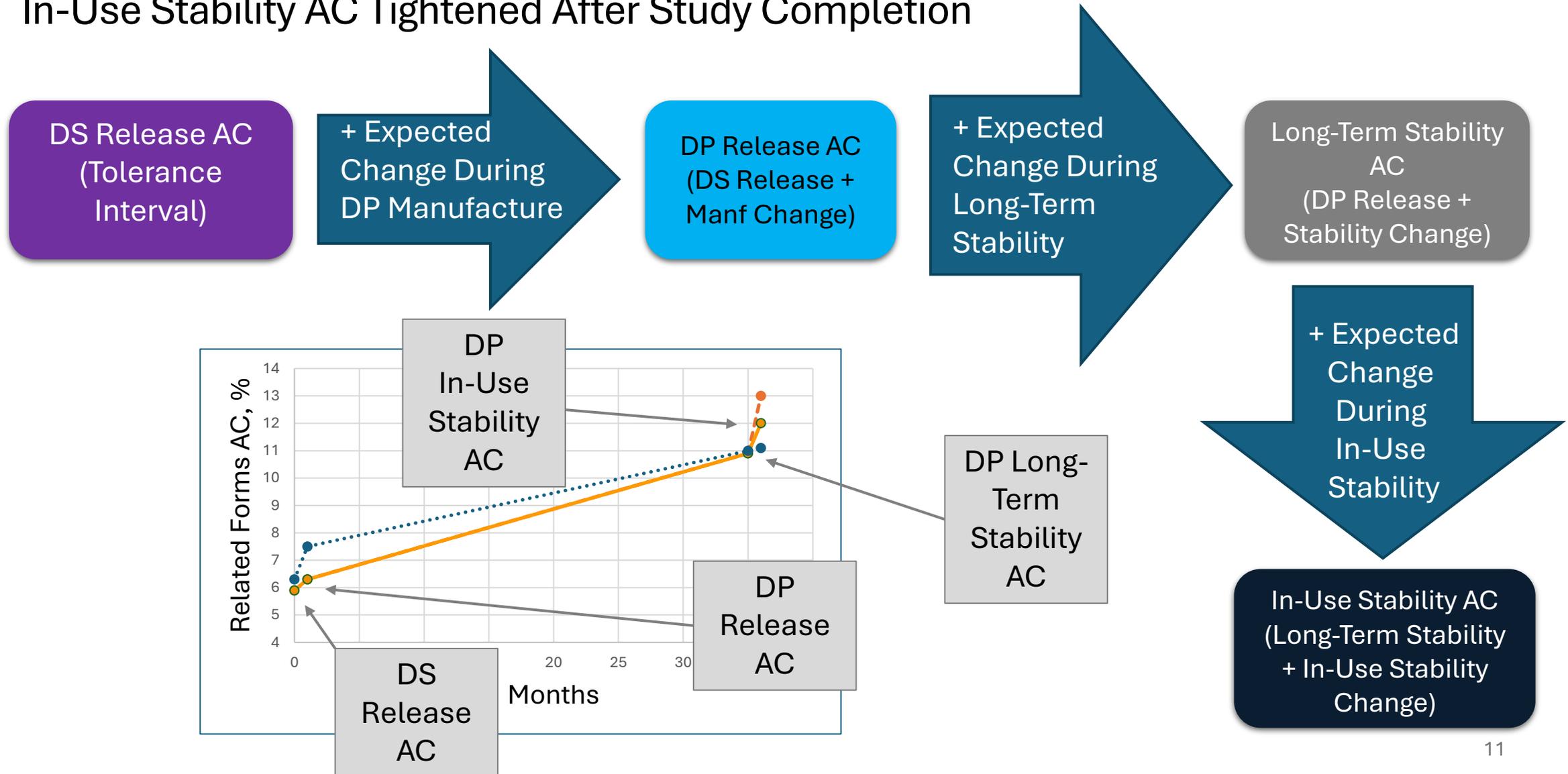
Example 2 - Proposal Approved at Time of Marketing Submission Approval

Post-Marketing Commitment Proposed



Example 2 - Post-Marketing Commitment AC Adjustment

In-Use Stability AC Tightened After Study Completion



Specifications & manufacturing consistency

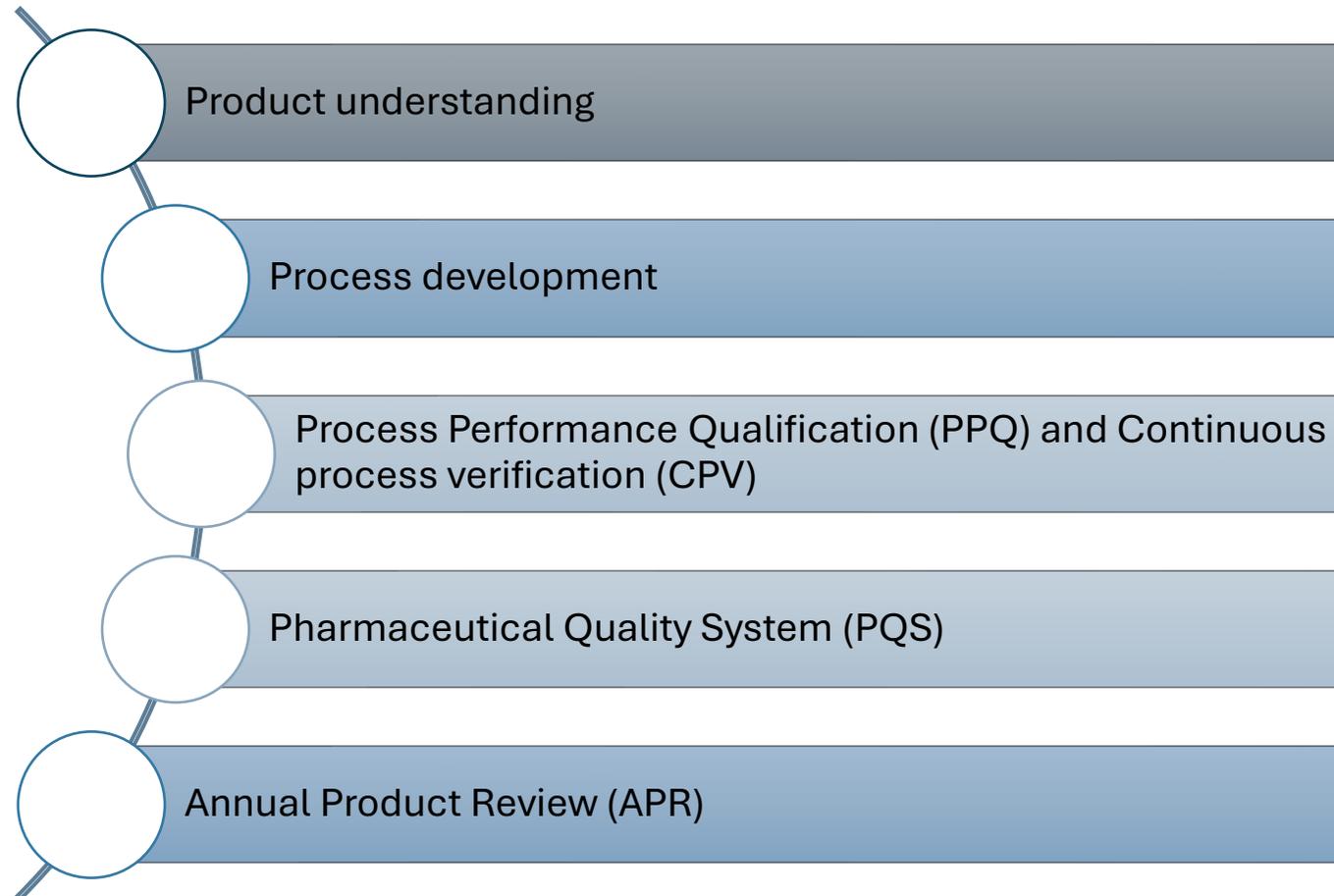
Extract from presentation of C. Campa "*Enhanced Pharmaceutical Quality System: Ensuring Confidence in Meeting Specifications*"

PDA India Chapter Quality Management Maturity Conference, 4-5 December 2025

Specifications & Manufacturing consistency

The specification is one part of the overall control strategy and is intended to control selected CQAs within ranges that are required to ensure safety and efficacy.

Other aspects are in place to justify and ensure process consistency and throughout the product lifecycle, including:

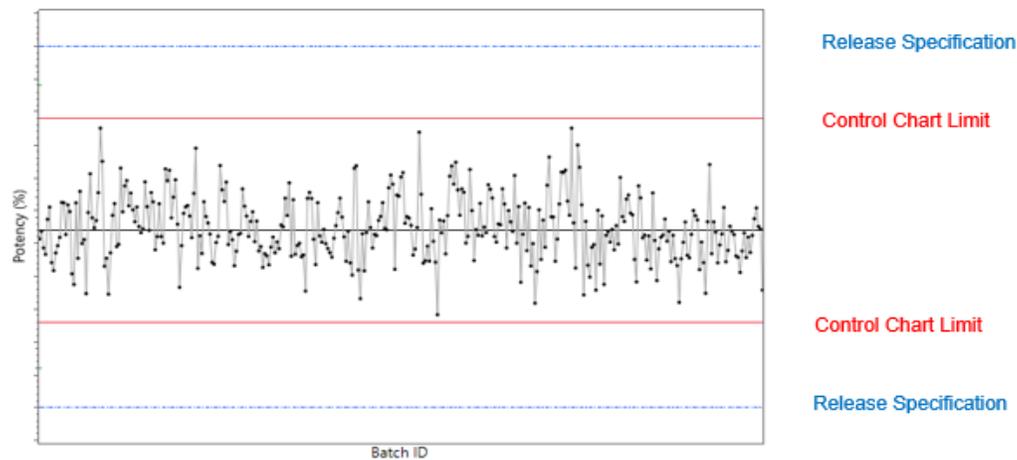


Illustrative wording to support consistency demonstration

- All **process validation** acceptance criteria for the critical controls, process intermediate quality attributes, and the drug substance release specifications, were met for the process validation runs
- In order to ensure that the manufacturing process remains in a state of control during commercial production, a **monitoring plan** has been established for routine production (process validation lifecycle stage 3).
- For the product quality data review, the drug substance release data is monitored against the **drug substance specifications, in addition to more stringent internal control chart limits within the Pharmaceutical Quality System (PQS)**.
- The **control chart limits** are used to monitor and **confirm process consistency** and help to distinguish between common cause and special cause variation. An excursion outside a control chart limit results in a deviation within the PQS with Quality oversight. The appropriateness of the control chart limits is assessed annually as part of the Annual Product Review (APR) program.
- Throughout the lifecycle of the product, **the drug substance specification acceptance criteria, which were established and justified based on clinical relevance / patient impact would not change unless driven by new clinical information**.
- However, the **control chart limits may be subject to change** based on an assessment of common cause variability using the available representative dataset.

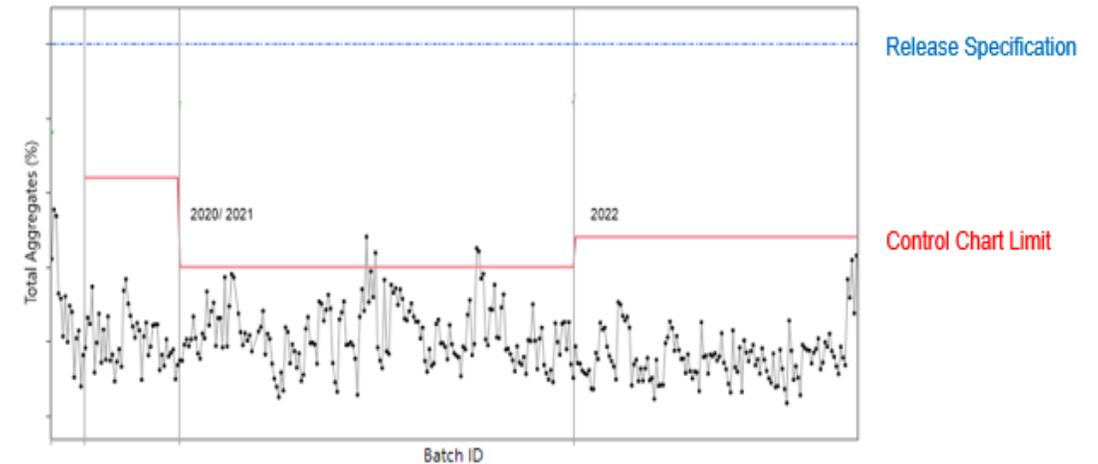
Potency

An example of product quality data monitoring is shown below for the Potency CQA for a commercial product. For the review period, all drug substance results are within the drug substance regulatory release specification acceptance criterion in addition to the control chart limits. The data set shows that the process is stable and predictable, and the control chart limits are appropriate to monitor process consistency.



Aggregates

As a result of the deviations in 2020-2021, an investigation was conducted within the PQS and determined the excursion outside of the previously established control chart limits was a result of common cause variability and no special cause was identified. For the 2021 APR, it was recommended to recalculate the control chart limits which were reflected in the control chart limit applied for the subsequent 2022 manufacturing campaign.



Acknowledgement

Slides on Specifications vs Manufacturing Consistency:

The EFPIA ICH Q6 support team

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