Enhanced Approaches to Setting Specifications – A Regulatory Perspective

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Health Canada Santé Canada

CMC Strategy Forum January 27, 2025

Canada

DISCLAIMERS

The views expressed in this presentation do not convey official Health Canada policy but are based on reviewer experience.

The information in this presentation relates to biotherapeutics.

OUTLINE

1. Explain the regulatory understanding of approaches to setting specifications for biologic drugs.
2. Describe the regulatory experience with assessing enhanced approaches to setting biologic drug specifications.
3. Share the regulatory thinking applied when enhanced approaches to setting specifications are used.
4. Outline regulatory expectations, filing requirements, and other considerations.

OBJECTIVES

Regulators – To better understand enhanced approaches to setting specifications.

Industry – To better understand the framework in which enhanced approaches are assessed.

Together – To initiate the relevant dialogue to work towards defining a consistent approach to expectations and assessment of enhanced approaches to setting specifications.

QUALITY REVIEW

Commercial specifications for a biotherapeutic product are a critical component of the overall control strategy that ensures safety and efficacy.

Drug substance and drug product specifications are only one component of the overall control strategy; the role of specifications is to confirm that other controls effectively deliver a product of appropriate quality.

REGULATORY UNDERSTANDING

For product attributes that are not defined by compendia, specifications must be established based on product and process understanding.

Traditional Approach – based on manufacturing experience at the time of the marketing application.

Enhanced Approach – based on knowledge and data that extends beyond manufacturing experience.

TRADITIONAL APPROACH

May not represent the true safety and efficacy of the drug and creates a challenge for both industry and regulators in defining and authorizing appropriate specifications that support the product lifecycle and supply to patients.

Establishing acceptance criteria based on manufacturing experience may result in limits that are narrow and lead to unnecessary batch rejection.

Establishing acceptance criteria based on statistical analysis of a limited number of batches may result in limits that are broad and lead to inappropriate lot release.

ENHANCED APPROACH

Comprehensive approaches are needed to define the most appropriate specifications.

Specifications should ensure that the product is safe and delivers the therapeutic benefit indicated in the label.

The resultant specification acceptance criteria may extend beyond the clinical and manufacturing experience.

ENHANCED APPROACH

Setting of specifications should consider all available data to ensure that decisions regarding the suitability of the product appropriately includes the line between rejecting lots that are likely to perform as expected and releasing lots that fail to meet the expectations.

The justification may be supported by additional sources of data.

REGULATORY EXPERIENCE

Data Source	Quality Attribute
Established or Published Limits: • Compendia • Guidance • Literature	particles, endotoxin, bioburden, host cell protein, host cell DNA, sterility, container closure integrity
Process and Product Knowledge Prior Knowledge	appearance, pH, osmolality, polysorbate, deliverable volume, break loose/glide force
Structure-Function, In Vitro, In Vivo, In Silico, Toxicology, Nonclinical, Dose Finding	charge heterogeneity, fragments, and high molecular weight species

REGULATORY EXPERIENCE

Data Models	Intended Purpose
Process Models	to justify product specifications
Stability Models	to support or set the proposed shelf-life
PK Models	to demonstrate a quality attribute have no impact on PK

REGULATORY EXPECTATIONS

The product control strategy is developed as part of the integrated control strategy using the principles outlined in ICH Q8, Q9, and Q10 guidelines.

The criticality of each control is appropriately justified and is aligned with the risk.

The acceptance criteria are defined to ensure product safety and efficacy while allowing for consistent manufacturing and adequate shelf life to support the supply chain.

REGULATORY FILING REQUIREMENTS

Provide a clear and well-supported rationale for why specific testing parameters, acceptance criteria, and quality attributes were chosen.

Include all relevant evidence to demonstrate the chosen specifications are appropriate for ensuring the desired quality and safety of the product.

OTHER CONSIDERATIONS

Describe your approach to setting specifications in a manner that we understand and can support.

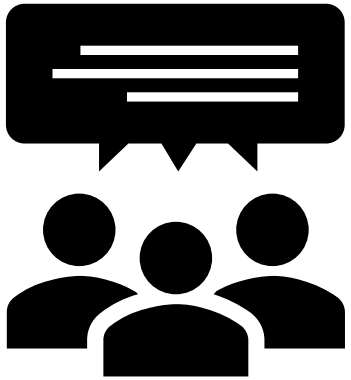
Early discussions can help shape the story that you need to tell.

If well supported, there should be no requirement to tighten product specifications based on future manufacturing data.

ACKNOWLEDGEMENTS

Karen Rowlandson – ICH Q6 EWG
Fiona Cornel
Wallace Lauzon

THANK YOU FOR LISTENING



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