# Regulatory Expectations for Data Models to Support a Market Application

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# 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 and predictive data models.

I am not a statistician or a subject matter expert in data models.

# OUTLINE

1. Explain the regulatory understanding of data models used to support a marketing application
2. Describe the regulatory experience with assessing data models.
3. Share the (current) regulatory thinking applied when data models are used.
4. Discuss the challenges with respect to data models.
5. Outline regulatory expectations, filing requirements, and other considerations.

# OBJECTIVES

Regulators – To better understand how data models are being developed and used.

Industry – To better understand the framework in which data models are assessed.

Together – To initiate the relevant dialogue to work towards defining a consistent approach to expectations and assessment of data models.

# DATA MODELS

Data models are increasingly used in many areas of biologic drug development.

It is recognized that data models are a powerful tool in biologic drug development and assist in expediting the development and authorization of critical medicines.

# REGULATORY EXPERIENCE

- Process Models
  - to justify product specifications
- Stability Models
  - to support or set the proposed shelf-life
  - to predict reference standard shelf-life
- PK Models
  - to demonstrate differences in quality attributes, have no impact on PK
  - to justify product specifications

# CASE STUDY

Share our regulatory thinking.

Outline our concerns and challenges.

# CASE STUDY

- Monoclonal antibody
- Priority review

- Release and stability acceptance criteria were justified using:
  - a predictive process model to justify release specifications;
  - and a stability model to support the proposed shelf-life.

# CASE STUDY – MODULE 3

## PROVIDED

- Description
- Model type
- Software
- Mathematical formulas
- Model parameters
- Data types

# CASE STUDY – REGULATORY THINKING

We are currently approaching the assessment of data models as we would an analytical procedure – **ICH Q2(2) / Q14**.

From a quality perspective we need *evidence* that the data model is suitable for intended purpose.

That *evidence* needs to demonstrate that the model is appropriately validated.

# CASE STUDY – REGULATORY THINKING

**CLARIFAX**

Provide evidence that the predictive process and stability models used to support the drug substance and drug product release and stability specifications are suitable for the intended use.

Your response should include evidence that the model is appropriately validated and evidence of model robustness.

# CASE STUDY – PROCESS MODEL

**ASSESSMENT**:

The simulated distribution for some attributes did not predict the observed distribution.

# CASE STUDY – STABILITY MODEL

**ASSESSMENT**:

Based on the goodness to fit statistic the stability model was considered only to likely support the change over the shelf-life for some attributes and did not support the change for other attributes.

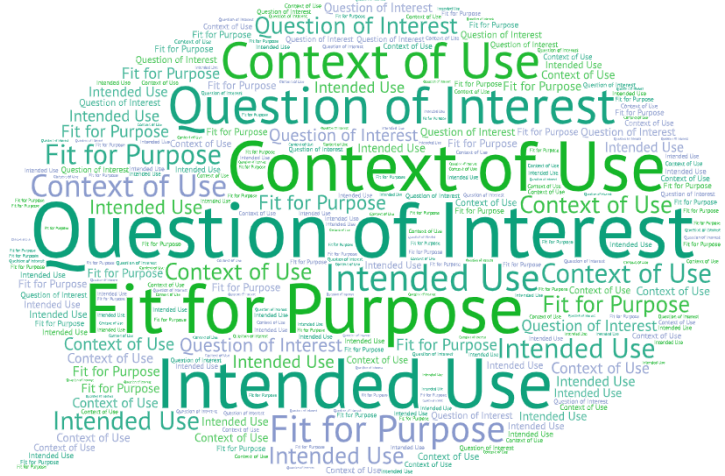
Out-of-specification (OOS) result at the 18-month timepoint for an attribute that was not included in the model.

# CASE STUDY – OUTCOME

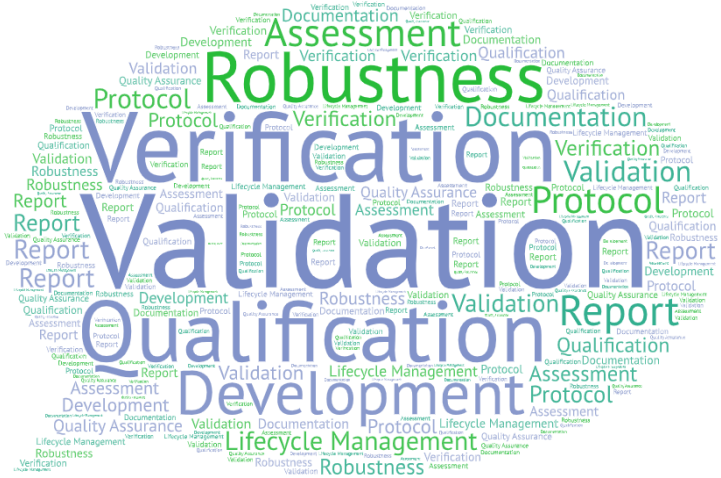
The sponsor was informed that the data models were not considered suitable for the intended purpose and were not considered in the final recommendation of the application.

Initiated the drafting of an internal guidance to outline the scientific and regulatory expectations for data models.

# THE CHALLENGE






# OTHER GUIDANCE

- **ASME V&V 40** (2018) – Assessing Credibility of Computational Modeling and Simulation Results through Verification and Validation: Application to Medical Devices
- **ICH M15** (Step 2) – General principles for Model-Informed Drug Development
- **FDA Draft Guidance** (2025) - Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products
- …

# REGULATORY EXPECTATIONS

## HEALTH CANADA

The data model is appropriately:

- developed,
- validated,
- and maintained.

The data model does what it is intended to do.

## OTHER

The data model is:

- verified,
- validated,
- and managed throughout the life cycle.

The data model is credible / applicable / adequate.

# FILING REQUIREMENTS

| HEALTH CANADA - BRDD | OTHER GUIDANCE |
|---|---|
| Intended Purpose | Question of Interest, Context of Use, Model – Risk, Influence, Impact |
| Description of the model, justification, development, and qualification. | Appropriateness of Model, Verification |
| Description and justification of dataset(s). | Comparator, Training Data, Tuning Data |
| Model performance parameters, criteria, and (validation) data that demonstrates that the model performs as intended. | Model Evaluation, Validation, Technical Criteria, Evidence Assessment, Applicability, Credibility |
| Lifecycle Management | Lifecycle Maintenance |

# ADDITIONAL CONSIDERATIONS

The expected maturity/performance of the model is commensurate with the intended purpose.

The stringency is which we assess the model will depend on the intended purpose.

# FINAL CONSIDERATIONS

- Tell us about the model in a manner that we understand and can support.
- Early discussions can help shape the story that you need to tell.
- Continue to use and file data models.
- Publish papers.
- Establish best practices.

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# THANK YOU FOR LISTENING

I look forward to further discussion.

## CONTACT INFORMATION

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