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SCIENCE MEDICINES HEALTH

# The EU Quality Innovation Group perspective on Modelling and AI in pharmaceutical process development and manufacturing

CASSS CMC Strategy Forum Europe, June 25th 2026

Presented by Leticia Martinez-Peyrat, Quality Assessor at ANSM and EMA QIG Member

ansm
French National Agency for Medicines and Health Products Safety

An agency of the European Union

# Disclaimer

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The presenter does not have any conflict of interest.

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# Modelling and Artificial Intelligence in CMC

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International Journal of Pharmaceutics

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## Quality by digital design in action: a workflow for crystallisation and isolation☆

Ian Houson [a,b], Humera Siddique [a,b], Magdalene W.S. Chong [a,c], Murray Robertson [a,b], Alice J. Turner [a,b], Alison Nordon [a,c], Amal Osman [a,b], Amparo Galindo [f], Andrew S. Dunn [a,b], Blair Johnston [a,b], Brahim Benyahia [a,d], Cameron J. Brown [a,b], Chantal L. Mustoe [a,b], Chris J. Price [a,e], Chris D. Reilly [a,d], Claire Adjiman [a,f], George Jackson [f], Elke Prasad [a,b], Gavin Halbert [a,b,g], Helen Feilden [a,b], Jan Sefcik [a,e], John McGinty [a,c], John Robertson [a,b], Kenneth Smith [a,b], Mais Al-Attili [a,b], Mark McGowan [a,b], Mariam Siddique [a,b], Momina Pathan [a,b], Nazer Rajoub [a,b], Niki Hamilton [a,b], Rachel Feeney [a,b], Scott Brown [a,c], Stephanie J. Urwin [a,b], Thomas Bernet [a,f], Thomas Pickles [a,b], Wei Li [a,d], Alastair J. Florence [a,b]

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## Quality by digital design to accelerate sustainable medicines development☆

Chantal L. Mustoe [a,b], Alice J. Turner [a,b], Stephanie J. Urwin [a,b], Ian Houson [a,b], Helen Feilden [a,b], Daniel Markl [a,b], Mohammed M. Al Qaraghuli [a,b], Magdalene W.S. Chong [a,c], air F. Johnston [a,b], Cameron J. Brown [a,b], nah Batchelor [a,b], Brahim Benyahia [a,c], iam [f], Javier Cardona [a,g], Ciro Cottini [h], ı W. Halbert [a,b,i], Mark Henson [j], Pirmin Hidber [k], [a,c], Jérôme Mantanus [m], John McGinty [a,g], Ottoboni [a,g], Elke Prasad [a,b], Per-Ola Quist [o], ı Rowland [q], Walkiria Schlindwein [r], ore Settanni [a,u],

European Journal of Pharmaceutics and Biopharmaceutics 224 (2026) 115080

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## AI/ML in drug product development & manufacturing - report on the 8th APV Winter conference

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ARTICLE INFO

*Keywords:*
Artificial intelligence
Machine learning
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Model output
Model accuracy

ABSTRACT

Artificial Intelligence and Machine Learning (AI/ML) have already revolutionized Drug Discovery. However, Chemistry, Manufacturing, and Controls (CMC) remains in "digital infancy". This report from the 8th APV Winter Conference with 55 participants details a critical industry shift toward Digital Design and Quantitative Formulation. Five cooperative shifts are necessary for this transformation: redefining scientists as orchestrators, democratizing computational fluency, prioritizing structured data, optimizing strategic experimentation, and aligning with evolving regulatory frameworks. Critical challenges like data reliability, model explainability, and "human-in-the-loop" accountability are addressed. Through case studies ranging from physicochemical profiling, formulation and process development, equipment design, manufacturing and analytical control, and biopharmaceutics, the conference demonstrated how AI/ML creates high-fidelity and interoperable architectures advancing drug product development and manufacturing.

Journal of Pharmaceutical Sciences 114 (2025) 1095–1107

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Pharmaceutical Biotechnology

## Qualification of mechanistic models in biopharmaceutical process development

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Model credibility
Uncertainty quantification
ASME V&V 40
Process characterization
Control strategy

ABSTRACT

Mechanistic process models play an increasingly important role in biopharm and manufacturing in supporting process design, characterization, and infor Despite the potential of mechanistic models, there is currently no clear conse their qualification, i.e. the processes of determining whether a model is suit in process development. In this work, a systematic and risk-based qualificat models in biopharmaceutical process development is introduced. The fram from other modeling frameworks and guidelines such as the ASME V&V 40 p ety of Mechanical Engineers (ASME) and preliminary considerations in proce Innovation Group (QIG) of the European Medicines Agency (EMA). Key conce are discussed using two case studies, including a model-informed optimizati filtration and diafiltration process and a model-informed control strategy step. The suggested framework can act as a foundation for dialogue and guid maceutical process development. It holds the capability to harmonize mode industry and establish an agreement on the qualification of mechanistic mode development.



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Review

## Empowering the pharmaceutical workforce for the digital future

Natalie Maclean [a], Susanna Abrahmsén-Alami [b], Catriona Clark [a], Frederik Dörr [b], Alastair Florence [a], Jarkko Ketolainen [c], Morten Lindow [d], Jérôme Mantanus [e], Jukka Rantanen [f,g], Gavin Reynolds [h], Amy Robertson [i], Daniel Markl [a,*]

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ARTICLE INFO

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Digital skills
Multi-disciplinary
Data science
Artificial intelligence

ABSTRACT

The pharmaceutical industry is undergoing a rapid digital transformation. These changes are reshaping drug substance and drug product development and manufacturing, creating both opportunities and challenges that span pharmaceutical sciences, data science, and automation engineering. However, significant skills gaps persist, limiting the sector's ability to fully leverage digital technologies and sustain innovation.

This paper explores the shifting digital and data science skills needs within the pharmaceutical industry, with a focus on industrial pharmacy and pharmaceutical sciences in the UK and Europe. We examine the key technological transformations reshaping the sector, the evolution of job roles, and the attributes required of the future workforce. Building on these insights, we propose an integrated approach to skills development that spans the entire career lifecycle – from embedding digital competencies in higher education to supporting lifelong learning through flexible, industry-aligned continuing professional development.

Addressing these skills gaps requires coordinated action from academia, industry, and policymakers. By fostering a collaborative, interdisciplinary, and adaptive learning ecosystem, the pharmaceutical sector can equip its workforce to thrive in a rapidly changing landscape and continue improving global health and wellbeing.

nature communications

Article

https://doi.org/10.1038/s41467-024-54011-9

## In silico formulation optimization and particle engineering of pharmaceutical products using a generative artificial intelligence structure synthesis method

Received: 31 March 2024
Accepted: 28 October 2024
Published online: 07 November 2024
Check for updates

Timothy Hornick[1], Chen Mao[2], Athanas Koynov[3], Phillip Yawman[1], Prajwal Thool[2], Karthik Salish[2], Morgan Giles[3], Karthik Nagapudi[2] & Shawn Zhang[1]

Pharmaceutical drug dosage forms are critical for ensuring the effective and safe delivery of active pharmaceutical ingredients to patients. However, traditional formulation development often relies on extensive lab and animal experimentation, which can be time-consuming and costly. This manuscript presents a generative artificial intelligence method that creates digital versions of drug products from images of exemplar products. This approach employs an image generator guided by critical quality attributes, such as particle size and drug loading, to create realistic digital product variations that can be analyzed and optimized digitally. This paper shows how this method was

# Modelling and Artificial Intelligence in CMC

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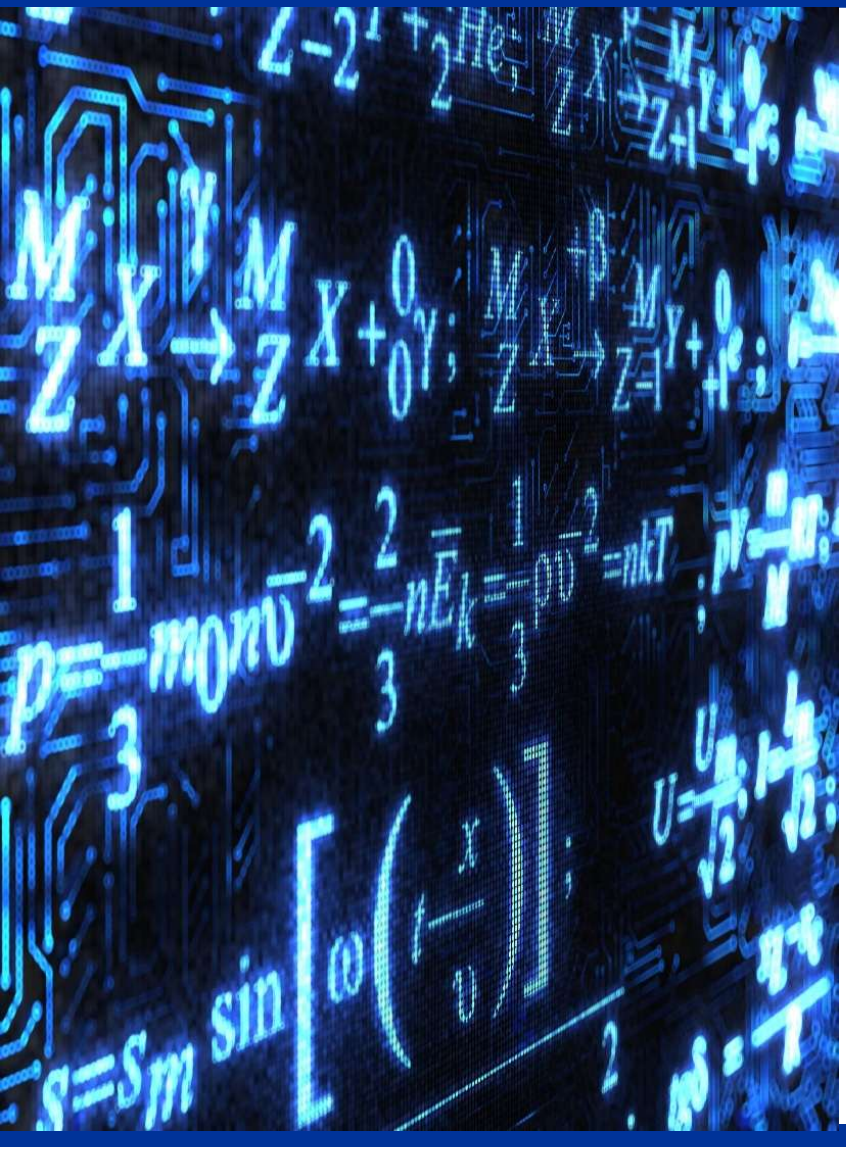

*"The application of digitalization and emerging technologies in the manufacture and control of drug (medicinal) products can lead to risk reduction, when such technologies are fit for their intended use. However, they can also introduce other risks that may need to be controlled."*

– ICH guideline Q9 (R1) on quality risk management
EMA/CHMP/ICH/24235/2006

# Use of AI across medicines lifecycle

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**New Pharma Legislation**
**EU AI ACT**

**EMA reflection paper on use of AI in medicinal product lifecycle**
**EMA/FDA 10 basic principles**

Revision of GMP Annex 11 (computerized systems) and Chapter 4 (documentation)
New Annex 22 (requirements for use of AI and ML in manufacturing)

Quality Innovation Group: preliminary considerations on process models

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# Use of AI across medicines lifecycle

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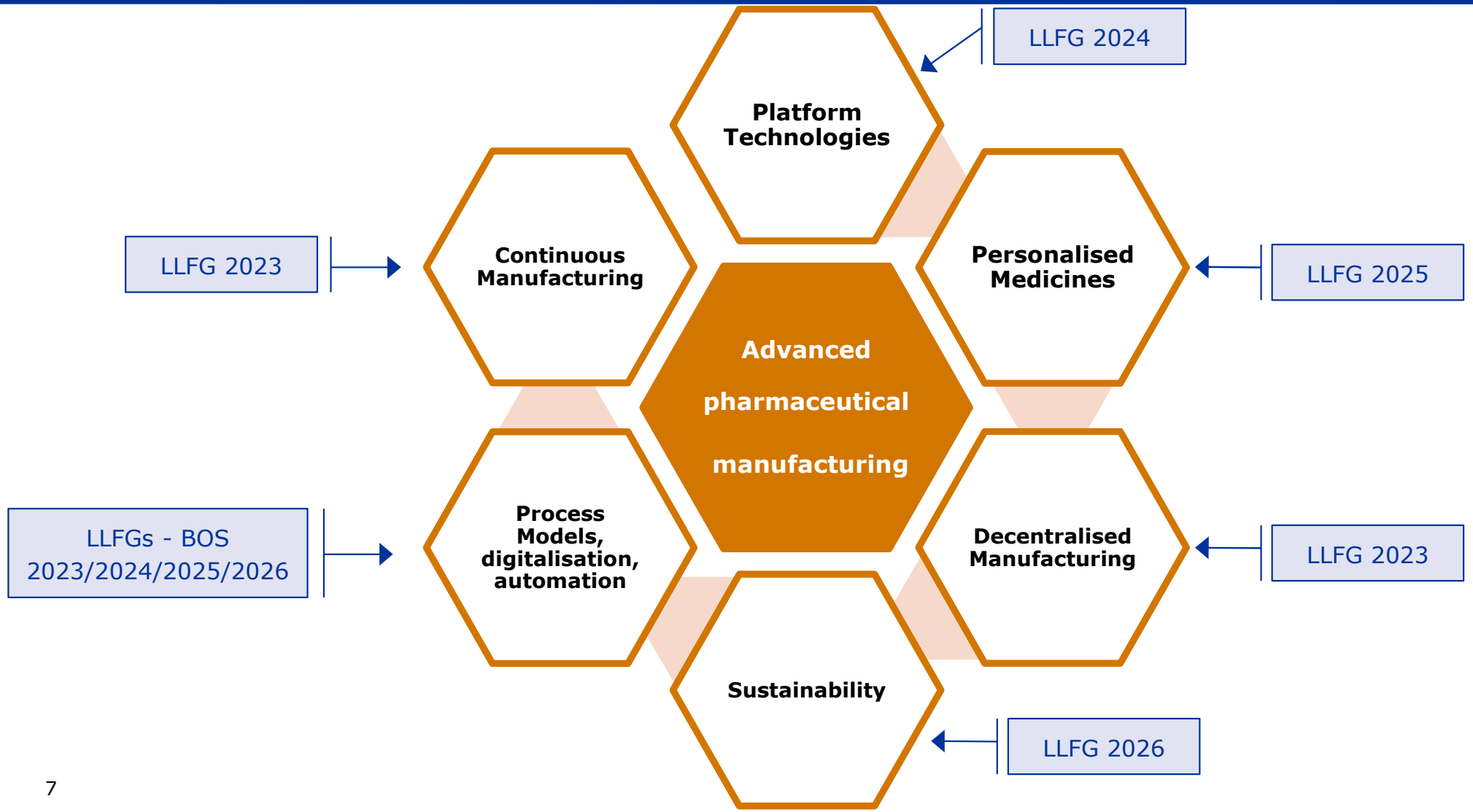
**Quality Innovation Group: preliminary considerations on process models**

# QIG main working areas



# QIG considerations regarding pharmaceutical process models

Preliminary QIG considerations

- First published in February 2024
- 1-month consultation period

LLFGs 2023/2024 and BOS 2025

Several 1-1 meetings

# Challenges and gaps

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- Flexible, risk-based regulatory framework
- Clear definitions and terminology
- Validation approach
- Model documentation
- Lifecycle management
- Human-in-the-loop concept
- Data governance and storage
- Global harmonisation
- Education and training

# QIG considerations regarding pharmaceutical process models

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- **Scope: mechanistic, data-driven and hybrid models**

- Model Risk
  - How should the model risk to product quality be estimated and documented?

- Model building and validation

- Model control strategy
  - Model core quality information
  - Model lifecycle

# QIG considerations regarding pharmaceutical process models

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- Scope: mechanistic, data-driven and hybrid models
- **Model Risk**
  - **How should the model risk to product quality be estimated and documented?**
- Model building and validation
- Model control strategy
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  - Model lifecycle

# Model risk to product quality

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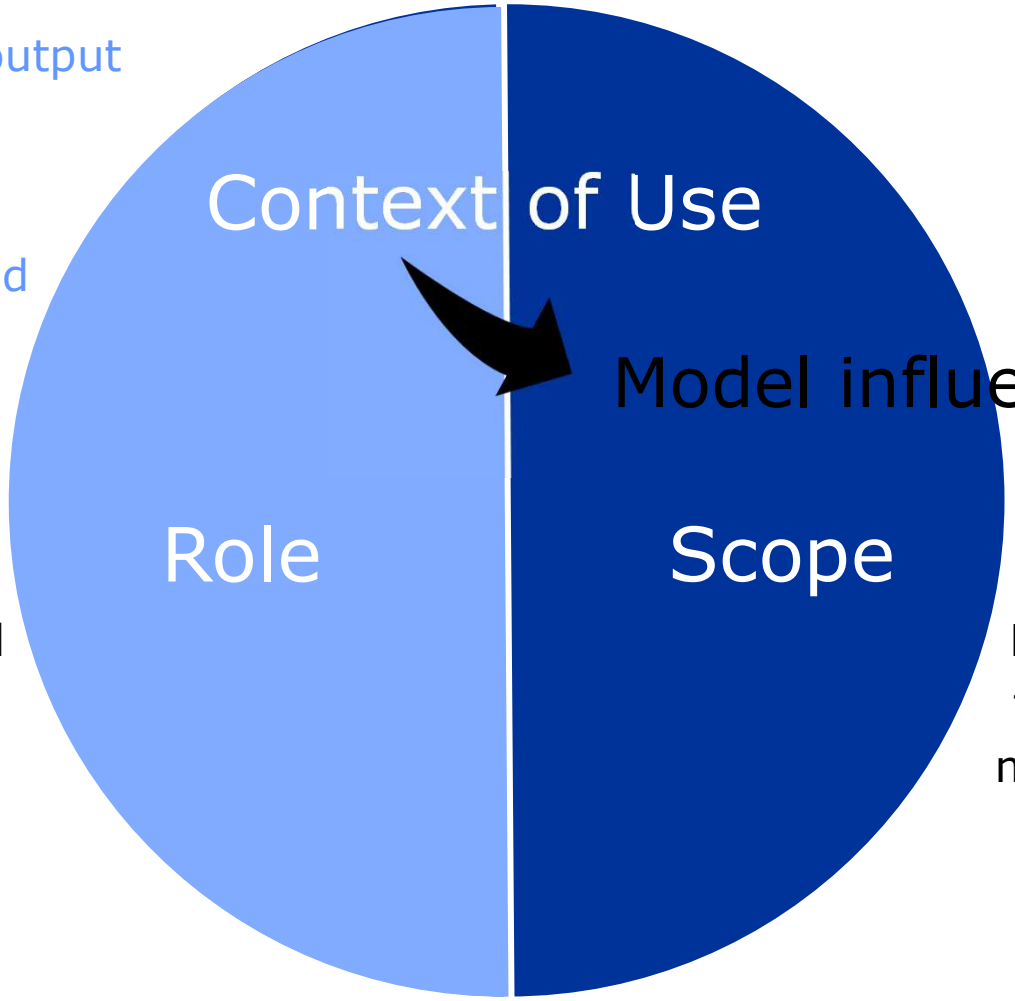
- criticality of the model output
- model implementation
- predicted output
- process/system modelled

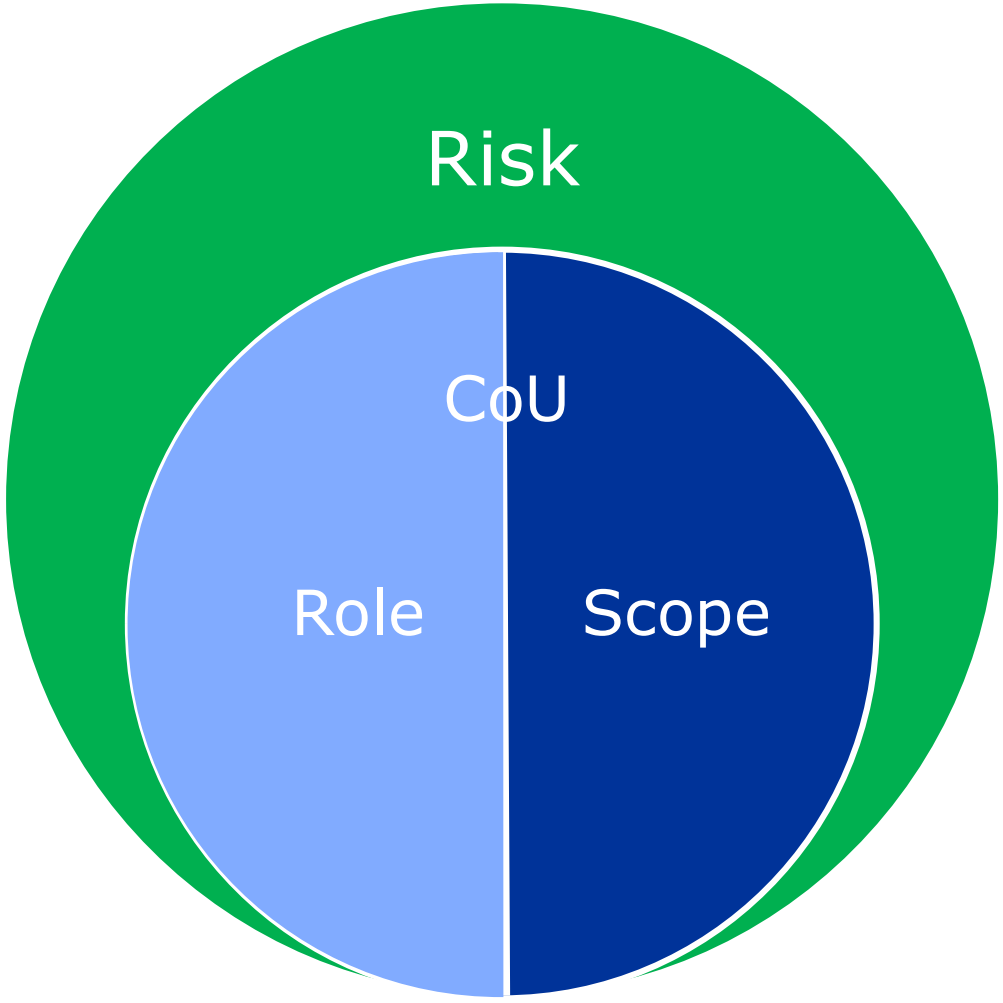


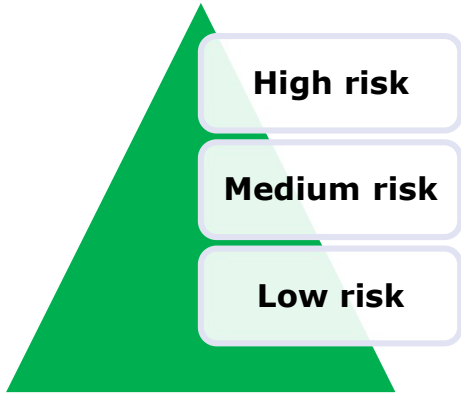

- release testing
- soft sensors
- PAT sensors
- in-process controls
- process boundaries

Describes the intended use of a model in the control strategy and in any decision-making process

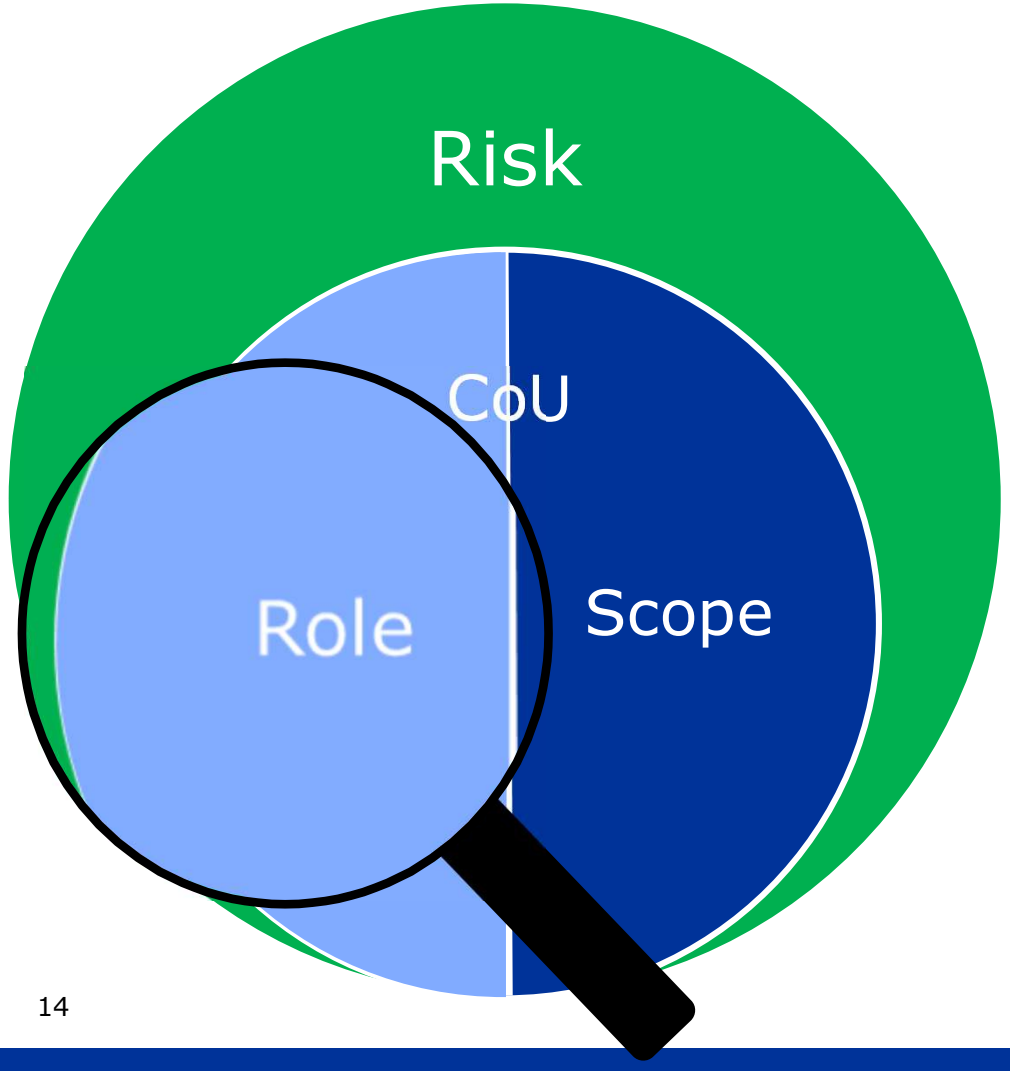
Describes if the model is the sole determinant for model output or impacted CQA(s), or if other information are used to inform decision-making

# Model risk to product quality



# Model risk to product quality



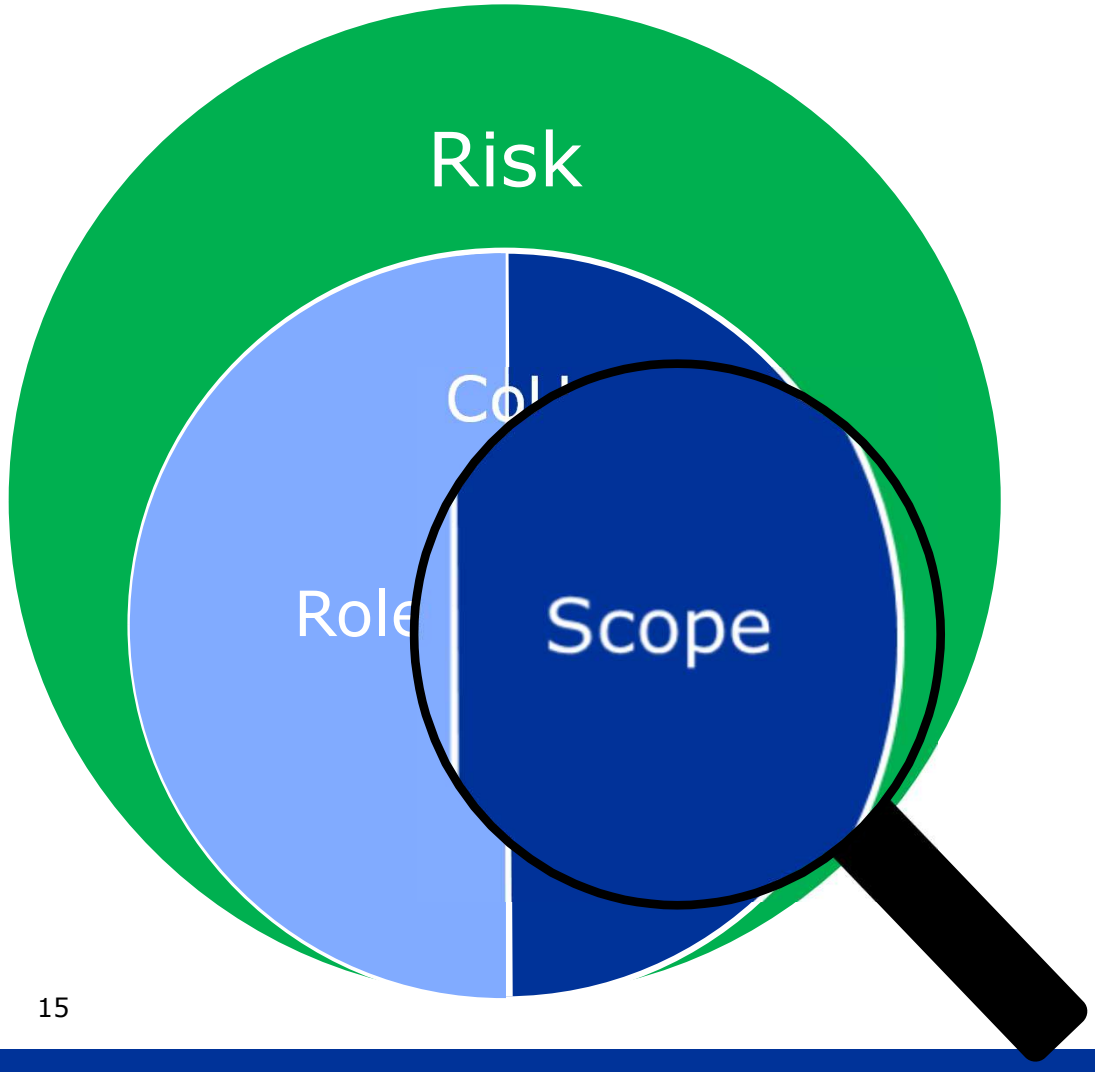

**Key questions**

☞ Is the model output used to control or adapt the process during routine manufacturing?

☞ Has the model been used to define process boundaries or limits?

☞ Is the model output a CQA/CPP or can the model impact a CQA?

# Model risk to product quality




**Key questions**

☞ Does the model replace end-product testing?

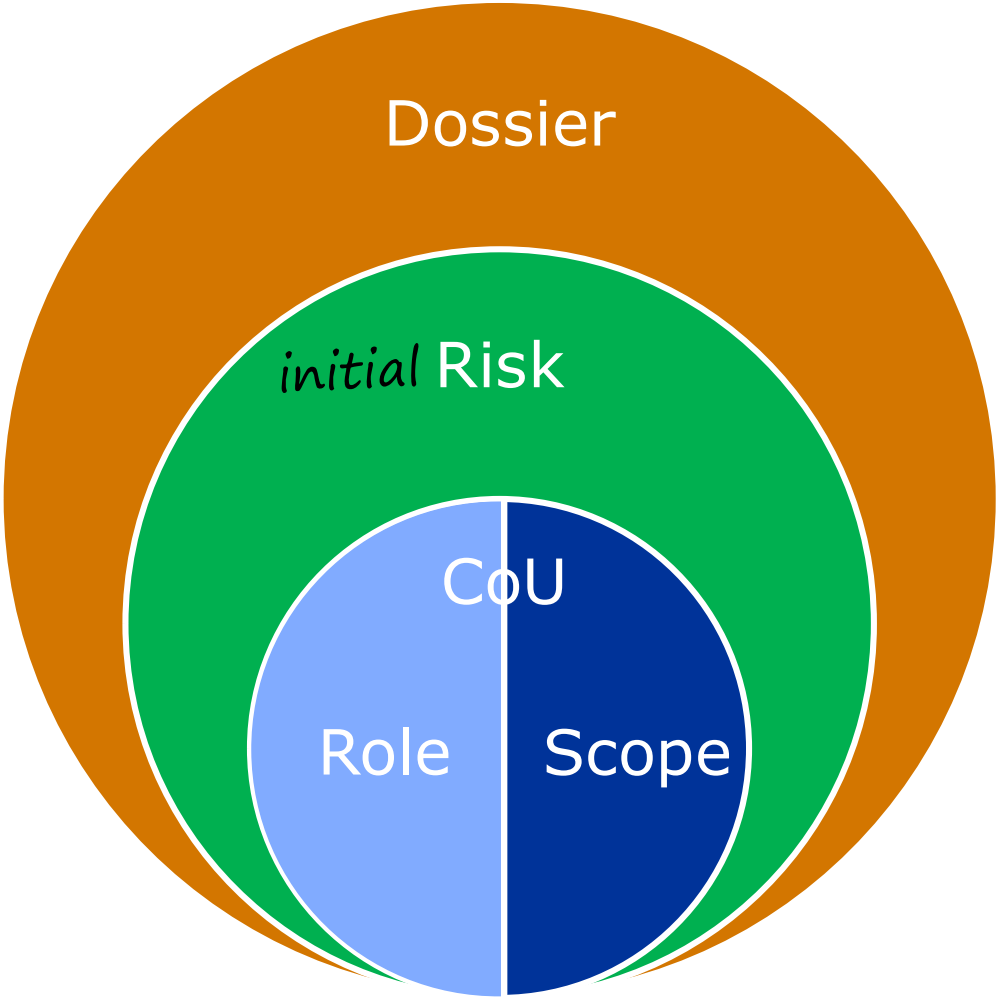
☞ Does the control strategy include additional control(s) for the predicted output or the impacted CQA(s)?

**Additional considerations**

☞ Consequence of a wrong decision?

☞ Likelihood of process failure?

# Model risk to product quality




*iterative process!*

# Experience with process models/AI in BIO

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- ✓ Use cases of process models and AI developments (mechanistic models, Machine Learning, Deep Learning, Digital Twin)
- ✓ Wide range of biopharmaceutical products (ATMPs and vaccines)
- ✓ Different CoUs (process design and characterization, optimization and scale-up, informed process control strategies, etc.)
- ✓ Examples classified as low or medium-risk models
- ✓ Not yet in submission files

# QIG considerations regarding pharmaceutical process models

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- Scope: mechanistic, data-driven and hybrid models
- Model Risk
  - How should the model risk to product quality be estimated and documented?
- **Model building and validation**
- **Model control strategy**
  - Model core quality information
  - Model lifecycle

# **Model building & validation** and **Model control strategy**

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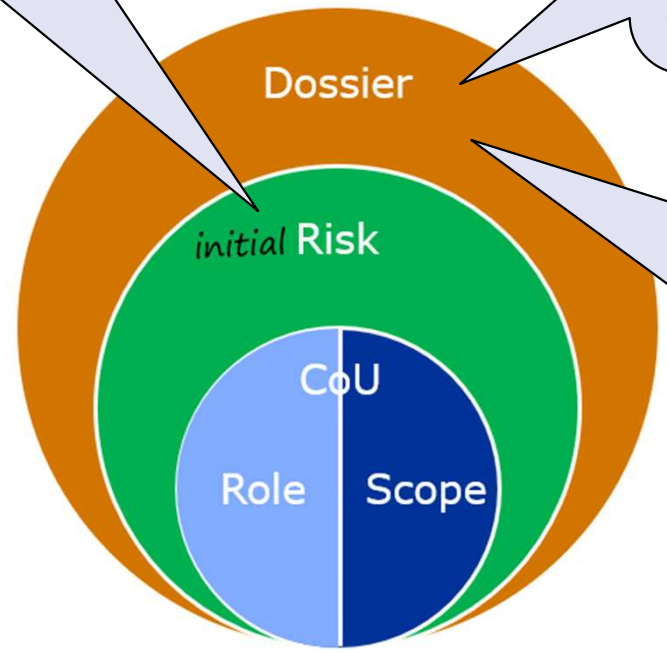
Only for medium and high-risk models

- Focus on model performance (accuracy, uncertainty) rather than model development
- Prior knowledge can be leveraged
- Only summary of validation studies and outcomes
- Continuous model verification across lifecycle




- Model core quality information: Set of information described in the dossier to support regulatory oversight and management of future model changes >> change to this information triggers a post-approval regulatory submission
- Post-Approval Change Management Protocols (PACMPs) can be leveraged

# QIG considerations regarding pharmaceutical process models

- Revised guidance to be published before the end of this year.
- Guidance will be updated as regulators gain experience with new types of models including AI-based models.
- Purpose of the QIG document is not to create a new EU standard.
- Intended to
  - translate commonly understood principles into a simplified and practical workflow,
  - assist regulators and stakeholders in dealing with process models,
  - give improved predictability regarding EU regulatory expectations.

# The beginning of a long journey

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- Still many areas for learning & discussion

   Level of regulatory notification associated with model updates

   AI/ML models: traditional validation versus continuous approach

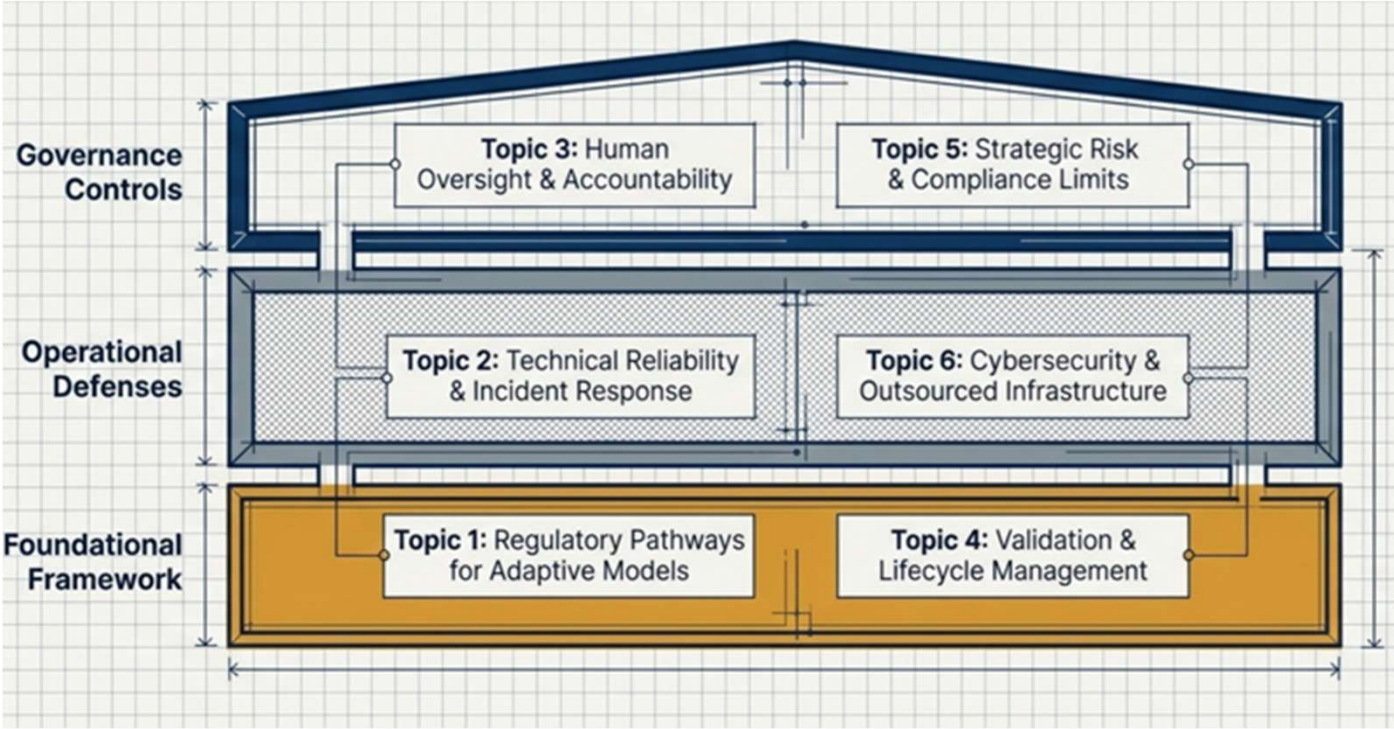
   Adaptive/self-learning models: additional challenges related to lifecycle changes and re-validation

- Need for applications with advanced modelling and adaptive control strategies in submissions ➔ testing and refining regulatory expectations and requirements 

- ICH Reflection Paper on Advanced Pharmaceutical Manufacturing – proposed ICH Guideline work to facilitate the adoption of advanced pharmaceutical manufacturing (26 January 2026) 

# What's coming next?

## Multistakeholder workshop on expert contributions to artificial intelligence guidance development (GMP Annex 22) – 30 June 2026




*The 6 pillars of AI guardrail architecture* – GMP Annex 22 Drafting Group

Briefing meeting with Interested Parties, April 2026 – Roberto Conocchia, EMA Inspections Office

# What's coming next?

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## QIG Follow-up meeting on Digitalisation and Artificial Intelligence in pharmaceutical manufacturing – 18-19 November 2026

**Digitalisation** (foundational technologies, infrastructure, and data-driven systems)

- Real-time release testing (RTRT) and PAT in continuous manufacturing
- Digital twins, hybrid modelling, and simulations for process optimisation and risk-based QbDD
- Blockchain solutions for data integrity and traceability in manufacturing/QC data flows and supply chain
- Integration of IoT, edge/cloud computing for real-time manufacturing/QC data processing and adaptive production
- Digitalisation for manufacturing and quality control of personalised medicines
- Digitalisation applications for sustainability optimisation (e.g., monitoring energy/waste, data collection infrastructures)

**Artificial Intelligence** (techniques involving learning, prediction, pattern recognition, or autonomous decision-making)

- AI/ML-driven predictive maintenance
- Generative AI / LLMs and machine learning
- anomaly detection
- QC analytics (e.g., PAT, spectroscopy)
- automated CAPA / deviation management
- AI-enabled solutions for data integrity and traceability (e.g., intelligent monitoring, anomaly flags in data flows)
- AI for manufacturing and quality control of personalised medicines (e.g., adaptive therapies, patient-specific optimisation)
- AI model validation, explainability (XAI), and lifecycle management
- AI for sustainability optimisation (e.g., predictive analytics for energy/waste reduction)

# Conclusion

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- Support to advanced manufacturing through digital technologies and AI-based control strategies, is strategic for EU.

- We are committed to support developers providing high level guidance and promote regulatory convergence working in a collaborative way with international partners.

- QIG will follow-up on this topic to provide guidance focused on the scientific considerations and to address the regulatory gaps.

Come to talk to us: Regulators, Academia and Industry should learn together:
QIG@ema.europa.eu

# Any questions?

## Further information

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