AIRIS Annual Meeting 2025

Regulation for AI, Together for Tomorrow

10-12 September 2025

Machine Learning Applications in Pharmaceutical Manufacturing - a safe space to deploy AI (?)

Ehab Taqieddin, F. Hoffman-La Roche

Disclaimer

The views and opinions expressed in the following PowerPoint slides are those of the individual presenter and should not be attributed to Roche, its directors, officers, employees, volunteers, members, chapters, councils, Communities or affiliates.

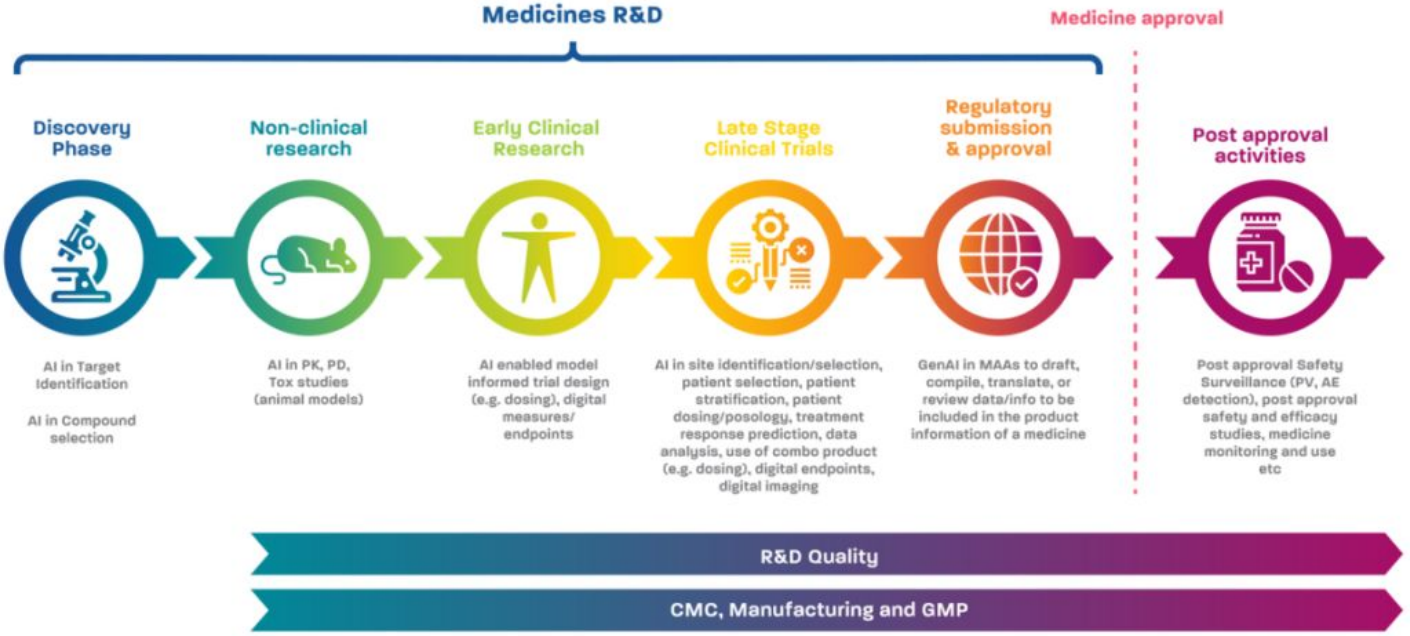
This presentation is incomplete without accompanying verbal commentary.

Table of contents

1. Artificial Intelligence use across the pharmaceutical life cycle & in manufacturing

AI in the Medicines Lifecycle

Adopted from EFPIA Position Paper*



*EFPIA Position Paper: https://www.efpia.eu/media/tzeavw1t/efpia-position-on-the-use-of-artificial-intelligence-in-the-medicinal-product-lifecycle.pdf

“Artificial Intelligence” in Pharma – Risk/Compliance/Regulatory Topics

“AI in Drug Development Life Cycle” *has different concerns than* ***“AI in Manufacturing”***

Patient/Medical Data Space

Among top compliance concerns are:

- *Data privacy*
- *Personal/medical data ownership*
- *Ethics (includ. Bias introduced by AI against certain parts of populations)*
- *Explainability of AI algorithms*
- *Documentation*
- *Life cycle management*

Manufacturing/CMC Data Space

Top regulatory/compliance topics are:

- ~~*Data privacy*~~
- ~~*Personal/medical data ownership*~~
- ~~*Ethics (includ. Bias introduced by AI against certain parts of populations)*~~
- ~~*Explainability*~~ *of AI algorithms*
- *Documentation*
- *Life cycle management*

Closer to technical and GMP compliance-related topics

Terminology is often different and confusing…

- *»AI vs. ML»,*
- *Digital Twin (of what?)*

2. AI and ML in pharma manufacturing – application examples

A) AI for clustering of information in continuous improvement
B) Machine Learning Models for mAb process predictions
C) Deep leaning algorithms to improve automated visual inspection

A.) GenAI Natural Language Processing (NLP) based clustering of deviations for continuous improvement

An AI tool for deviation clustering and analysis

Problem statement:

- In large manufacturing networks, there is a wealth of information to be data-mined for continuous improvement
- Manual study of free text fields is very labor intensive

What is NLP-based clustering and How Can It Improve Manual Processing?

- For deviations, one can use textual data (like titles and descriptions) to extract key topics and cluster similar deviations. => known as topic modeling, is a part of NLP.

Part of a larger set of applications around GenAI generating or analyzing text

- Many applications of «AI» in Pharma manufacturing and technical development use **Large Language Models** for text
  - Regulatory: Content generation for dossier, Q&A analysis
  - Quality: Improvement of reporting through suggested categorization
  - Technical development: Report generation, advanced search and knowledge mgmt

B.) Machine-learning models to predict mAb batch yield

An AI tool for improving planning and scheduling

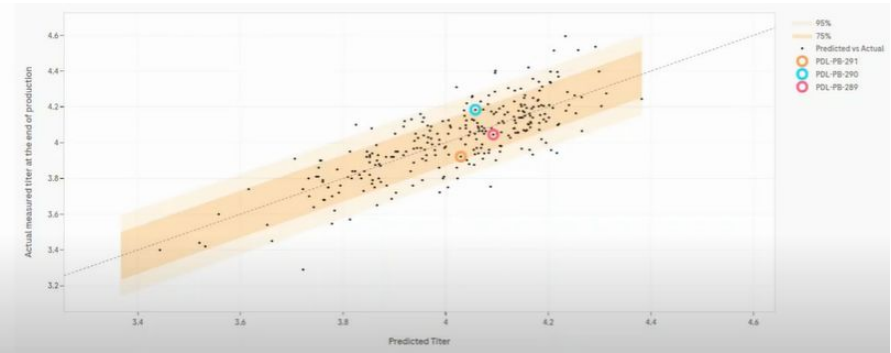
Problem statement:

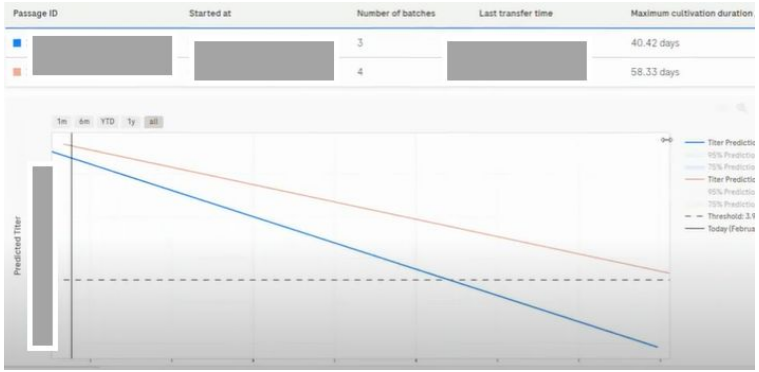
- In large scale mAb DS production, there is an inherent variability in the process, resulting in variability of processing times etc.
- The experiences gained with a product made over the lifetime of manufacturing is not easily translatable into actionable knowledge

Digital model of a manufacturing process

Could be of entire process or individual steps

- Here: prediction of titer/yield for mAb DS process

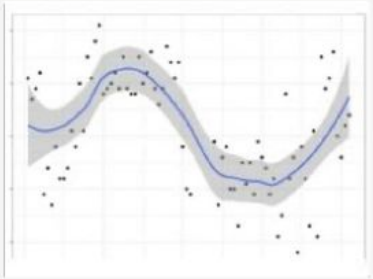




B.) Machine Learning in Digital Twins for Process Monitoring

Most modeling approaches can use machine learning algorithms

Problem statement



Yield variability of drug substance manufacturing between 4-25%, reasons typically unknown

Use case description

Predictive apps provide suggestions to operators:
a) Ideal batch sequencing depending on actual performance
b) Prediction of ideal timing for transfer to next process
c) Process parameter optimization (within validated ranges)

Highlights

5-10%
yield/titer increase

10%
yield drop recovered

>70%
Accuracy of titer prediction during initial "seed" process stage

2023 Manufacturing Leadership Awards

Predictive analytics application are scaled across drug substance sites and expanded to products that are still in development

C.) ML Deep Learning Models to improve automated visual inspection

ML algorithms improve quality assurance of parenteral product inspection

Problem statement:

- 100% in-process inspection of parenteral products – followed by a lab-based AQL test of a subset of samples - is a regulatory requirement
- Manual (human operator) based visual inspection is well established, but can be a bottleneck
- Automated visual inspection (AVI) with conventional algorithms can produce a significant amount of false positives

Advances in deep learning offer reduced classification error rates.

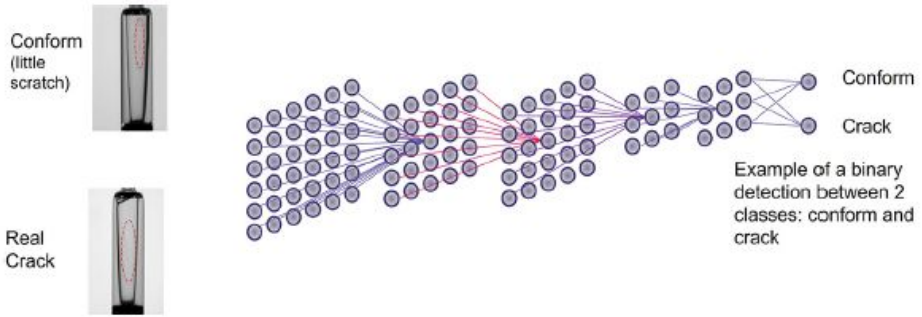


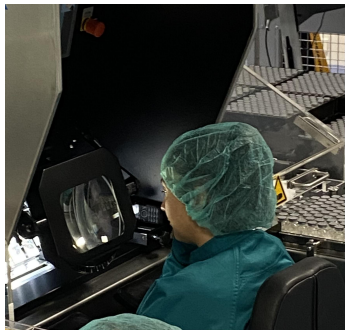
Image source: PDA Journal of Pharmaceutical Science and Technology, Vol. 77, No. 5, September--October 2023

C.) Visual Inspection Algorithms powered by Deep Learning

Reality today, potential for autonomous learning tomorrow

Camera-based Visual Inspection, powered by Deep Learning/neural network algorithms for image processing

From here...



..No AI....

..via AI....

...to here

Challenge: High false reject rate

- Requiring manual re-inspection
- Delayed product release
- Potential loss of good product

Sources:Muffin photo:https://medium.com/@ahffank/solving-the-famous-problem-of-puppy-vs-muffin-using-a-simple-web-application-on-google-app-a3264e2be49c
https://www.wilco.com/visual-inspection/camera-based-visual-inspection/

3. Emerging regulatory guidances and interest in Manufacturing Use

AI/ML- Recent Regulator's Interest - FDA

Drugs Space

- CDER Framework for Regulatory Advanced Manufacturing Evaluation (FRAME) Initiative
  - AI/ML in Manufaturing 1 of 4 priority topics
- 2 Discussion Paper
  - "**AI in Drug Manufacturing**" (March 2023)
  - "Using **AI & ML in the Development of Drugs & Biological Products** (May 2023)
- Meeting report of **FDA/PQRI workshop** on of Artificial Intelligence **in Pharmaceutical Manufacturing** (September 2023)
- September 2024
  - FDA "Digital Health & Artificial Intelligence Glossary"
- January 2025 **"Considerations for use of AI..in regulatory decision making"** (CDER Draft guidance)
  - Inclusive of all aspects of AI in pharma, including manufacturing uses
  - **Very prominent use of manufacturing/CMC context and examples**

Recent Regulator's Interest - Europe & International

- EMA «**Reflection Paper on the use of AI in the medicinal product life cycle**»
  - Draft 2023 – final version September 2024
  - Inclusive of manufacturing uses of AI (high-level only)
- EMA Quality Innovation Group
  - 2nd **«Listen & Learn» Focus Group October 2023**,Topic «Digital»
    - 2 day focus group with industry and other stakeholder representation
    - Application examples in two areas, 1.) Digital Twin/Process Modeling, 2.) ML to enhance existing specific GMP relevant applications
  - **«Preliminary Considerations on Process Models» document (March 2024)** contains a reference to AI powered process models
- EU Annex 22 on AI
  - Most recent publication from Europe, also jointly with PIC/S
  - Expectations on use of AI for GMP use

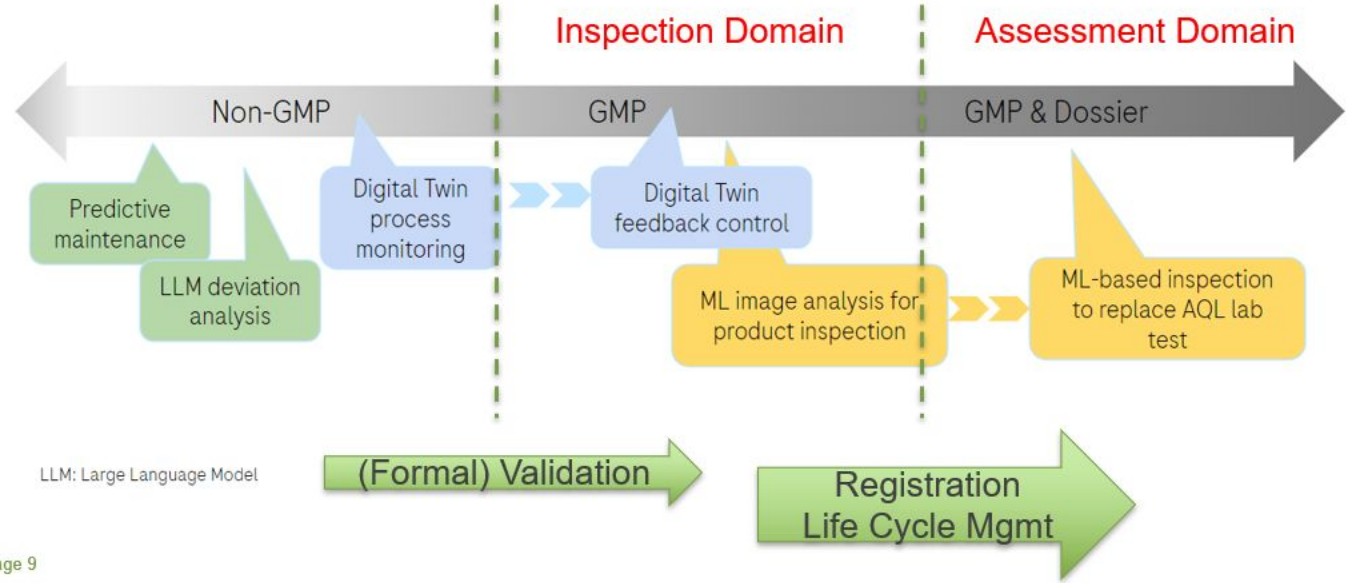
- ANVISA **«Regulatory Science and Innovation Summit» Oct 2024**
  - Innovation and Artificial Intelligence Session
- **WHO inspector consultation in 2023 with «Advanced Manufacturing» Topics**
  1. Continuous Manufacturing
  2. Artificial Intelligence in Manufacturing
     - WHO might consider «Points to consider» guidance for inspectors

4. Deeper dive on regulatory considerations around use of AI and ML in manufacturing

Current state of discussion:
The Compliance & Regulatory Spectrum of AI and ML

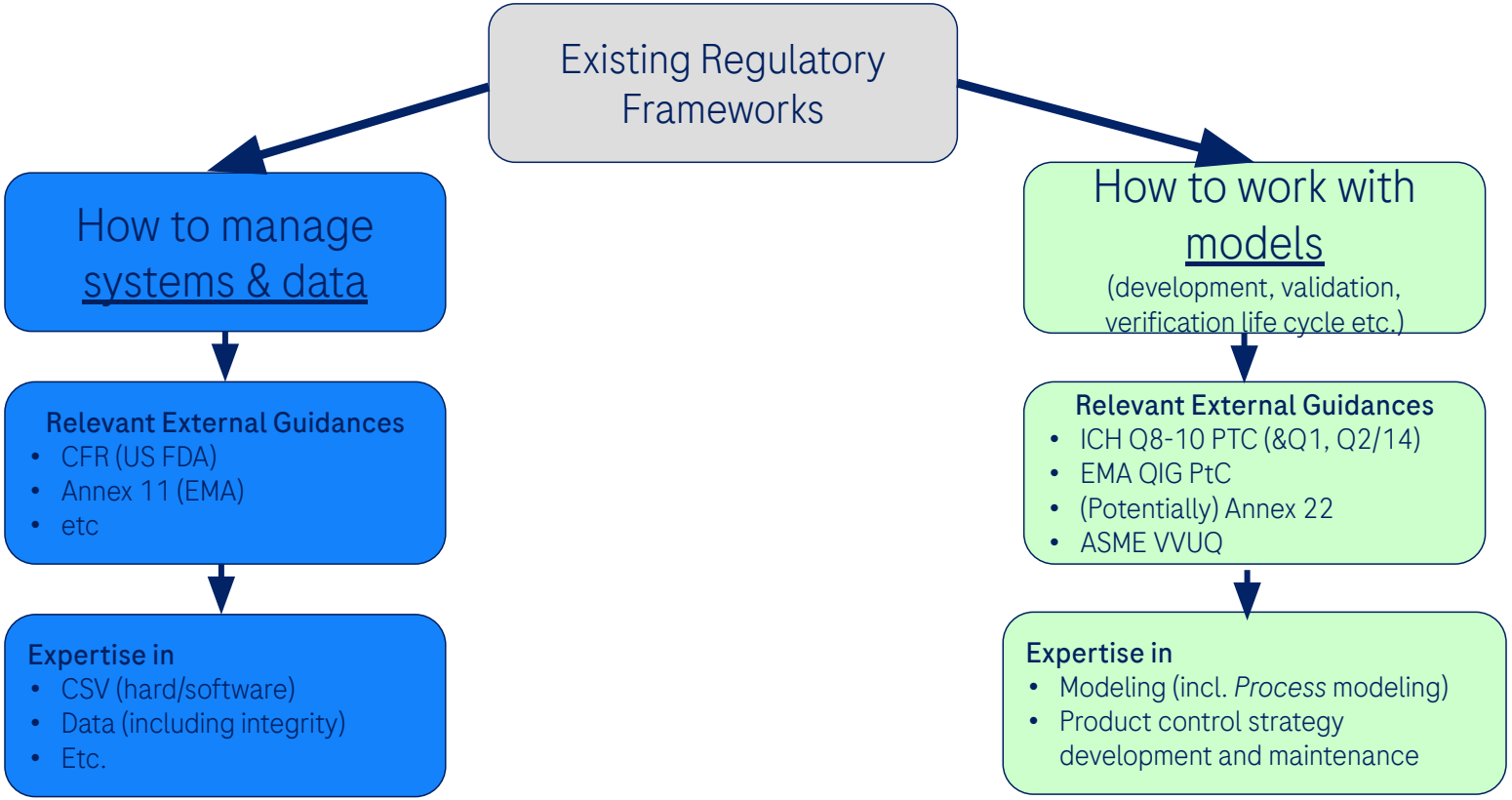
From a practitioners perspective, the question of mapping different AI applications on the spectrum of regulatory decision making, i.e. are they even GxP relevant and if they are GxP, are the registratoin relevant?

- The freedom to operate along the Regulatory/Quality Continuum….can depend on the usage



«AI» Regulatory topics map largely into two areas of existing regulation

Interpretation/adaption vs. new creation



Closing Remarks

- The use of Artificial Intelligence and Machine Learning are promising new tools
  - Also for applications in the regulated manufacturing space
- Pharmaceutical Manufacturing could be a «safe space to deploy AI»
  - Due to different nature of data in manufacturing vs. many other areas in Pharma
  - With and already existing strong regulatory framework
- There are many enabling regulations to AI which require merely an interpretation or expansion of scope to include AI
  - Some unique features of AI deserve forward looking attention to allow to use the full technical potential of the technology
- Global harmonization – in an evolving area like AI from the get-go – is key to adoption of AI in pharmaceutical manufacturing

Questions?

Doing now what patients need next