

RACI 2025

3 A 5 DE OUTUBRO

Blue & Green Tróia Design Hotel

The future-proof Industrial Pharmacist:
Thinking ahead & ready to act

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Conselho do Colégio de Especialidade
de Indústria Farmacêutica da Ordem
dos Farmacêuticos

3 a 5 de outubro 2025

Ordem dos Farmacêuticos, Lisboa



Demystifying AI for Pharmaceutical Manufacturing

toni.manzano@aizon.ai

Biomanufacturing: Product and process under control

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Manufacturing Science

The body of knowledge available for a specific product and process, including critical-to-quality product attributes and process parameters, process capability, manufacturing and process control technologies and quality systems infrastructure.

(Source: PhRMA Quality Technical Committee, 2003)

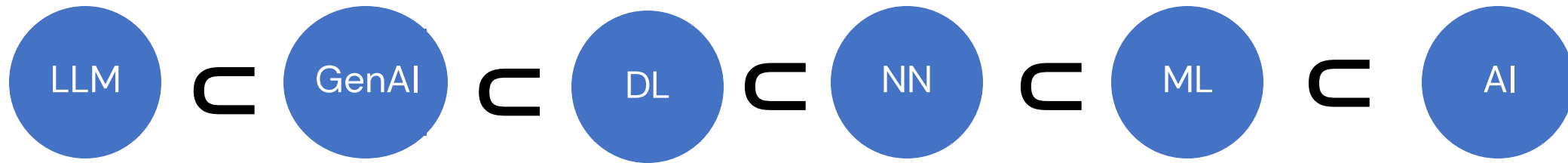
PAT

(...) The applicant should demonstrate an enhanced knowledge of product performance over a range of material attributes, manufacturing process options and process parameters

(...) Real-time quality control, leading to a reduction of end-product release testing

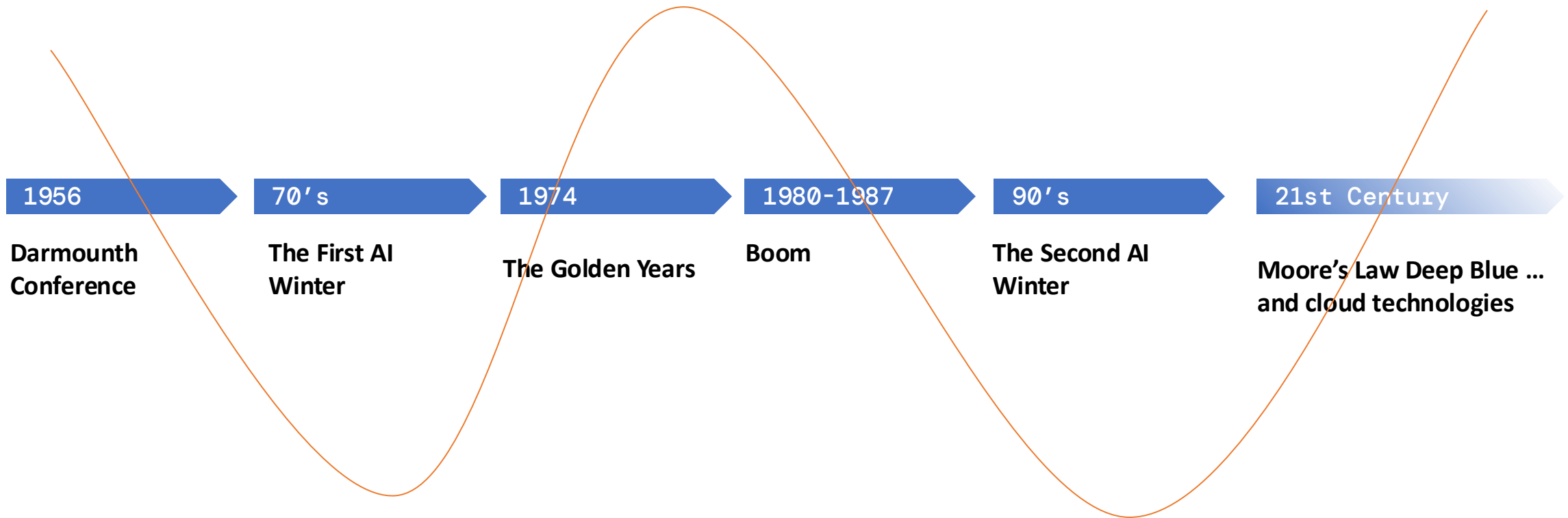
(...) A monitoring program (e.g., full product testing at regular intervals) for verifying **multivariate prediction models**

(Source: ICH Q8 step 4, 2009)



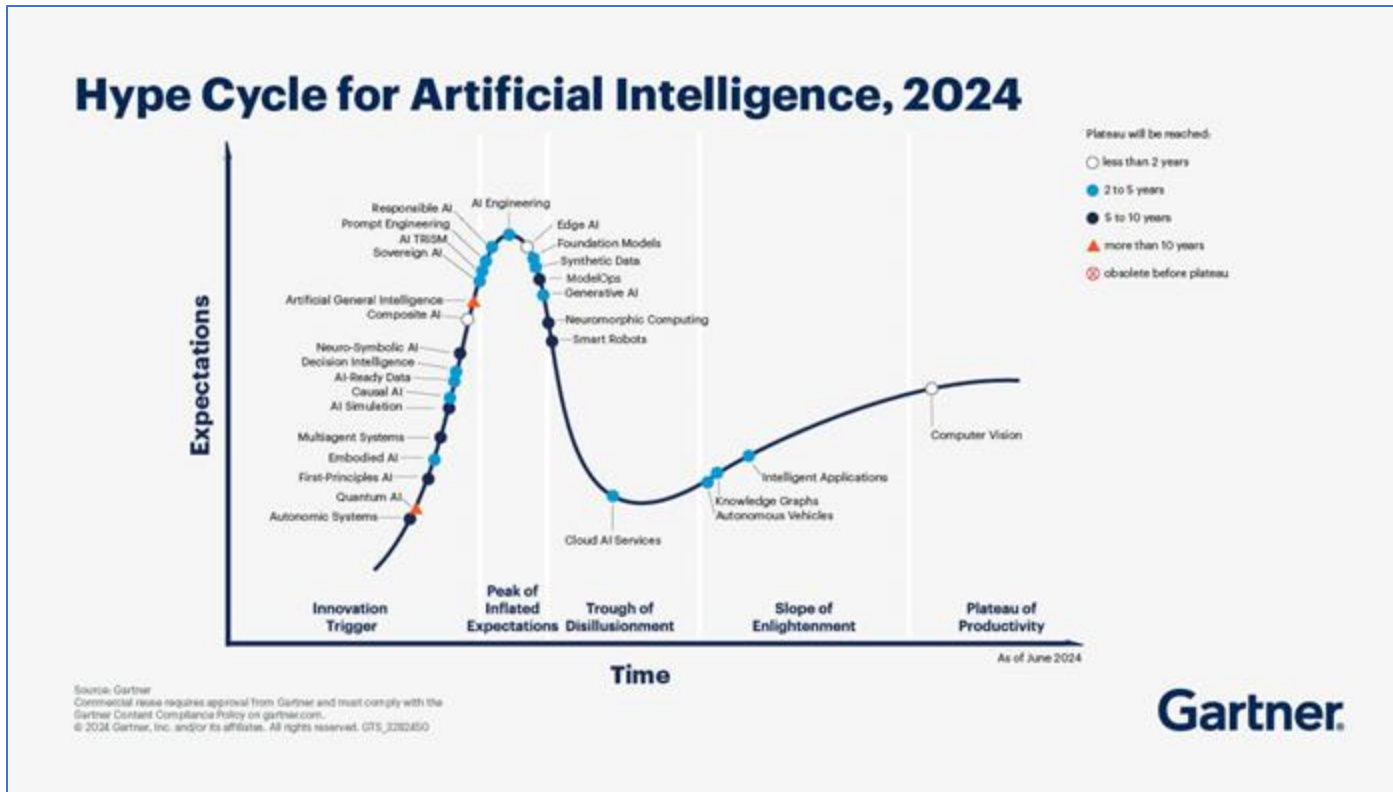
A brief history of AI: It's a hype now, but It has a come a long way...

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2025: the year of GMP AI

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Regulatory Tailwind

AI Awareness and Momentum

GMP AI Technology Availability

Batch Record Digitization Acceleration

SOURCE: HYPE CYCLE FOR ARTIFICIAL INTELLIGENCE, 2024, GARTNER | ADVANCED MANUFACTURING TECHNOLOGIES DESIGNATION PROGRAM, 2024, FDA | CONSIDERATIONS FOR THE USE OF ARTIFICIAL INTELLIGENCE TO SUPPORT REGULATORY DECISION-MAKING FOR DRUG AND BIOLOGICAL PRODUCTS, 2025, FDA

Who first imagined AI?

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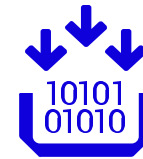
What is AI, really?

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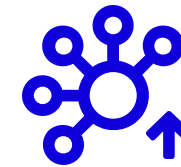


Data

Algorithm



$$Y_i = \lambda_i \circ F(x_i, Y_i)$$



Model

The 5 Basic Concepts in AI

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Training/Test Data

- Problem dataset

Algorithm

- Mathematical procedure that creates the model from training data

Model

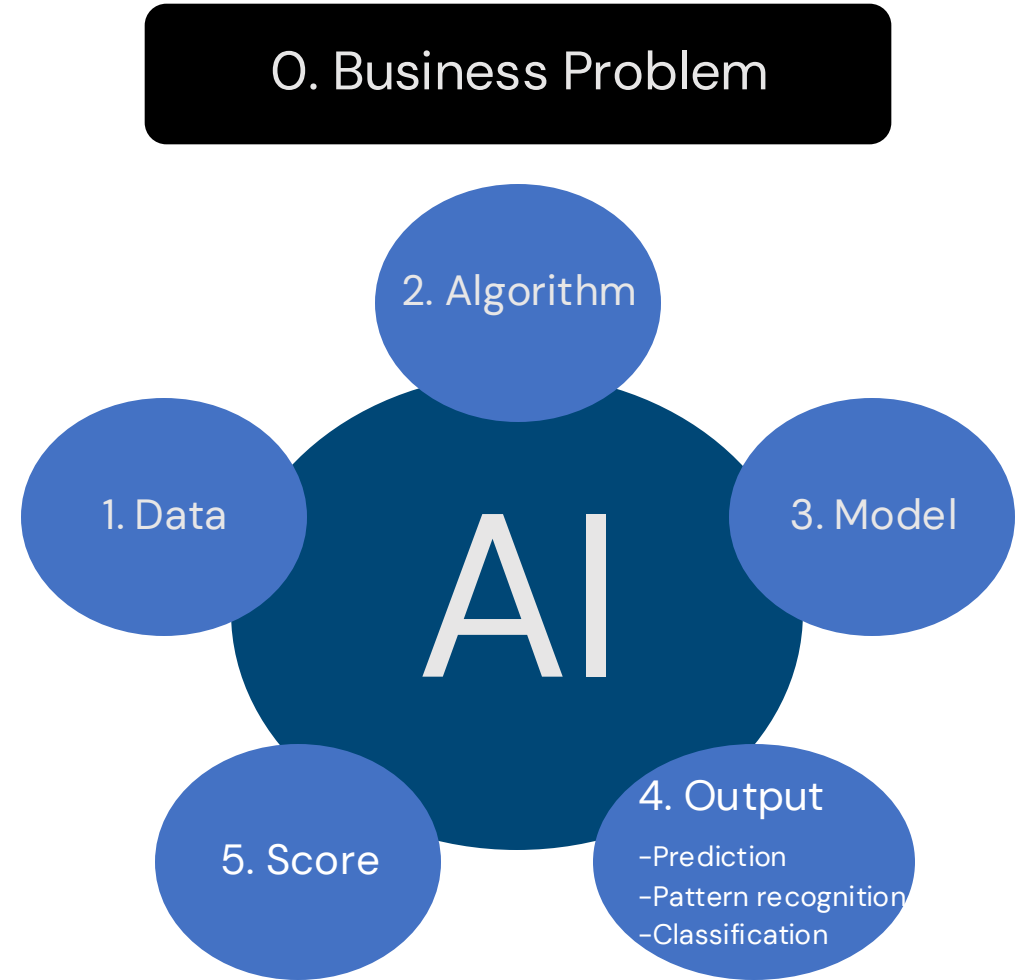
- Mathematical system that has been created from the exploration of a dataset; created after an extensive learning process referred to as training

Prediction / Classification / Recommendation / Recognition / Dimension Reduction

- Single inference over a model with an unseen sample

Evaluation

- Score evaluation of the test dataset



What Really is ML?

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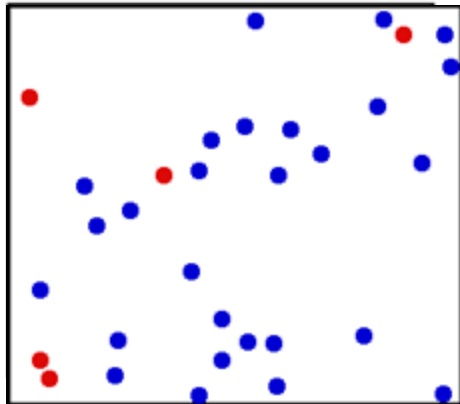
Classic mechanics



$$\frac{(p_1 - p_2)}{\rho l} < F_\gamma \cdot x_T \rightarrow$$
$$Q_a = \frac{1}{8} \cdot 4.17 \cdot C_v \cdot p_1$$
$$\cdot \left(1 - \frac{p_1 - p_2}{(3F_\gamma \cdot x_T)}\right) \cdot \sqrt{\frac{p_1 - p_2}{(T_a + 273.15)}}$$

$$\frac{(p_1 - p_2)}{\rho l} \geq F_\gamma \cdot x_T \rightarrow$$
$$Q_a = \frac{1}{8} \cdot 0.667 \cdot 4.17 \cdot C_v \cdot p_1$$
$$\cdot \sqrt{\frac{p_1 - p_2}{(T_a + 273.15)}}$$

Statistical mechanics



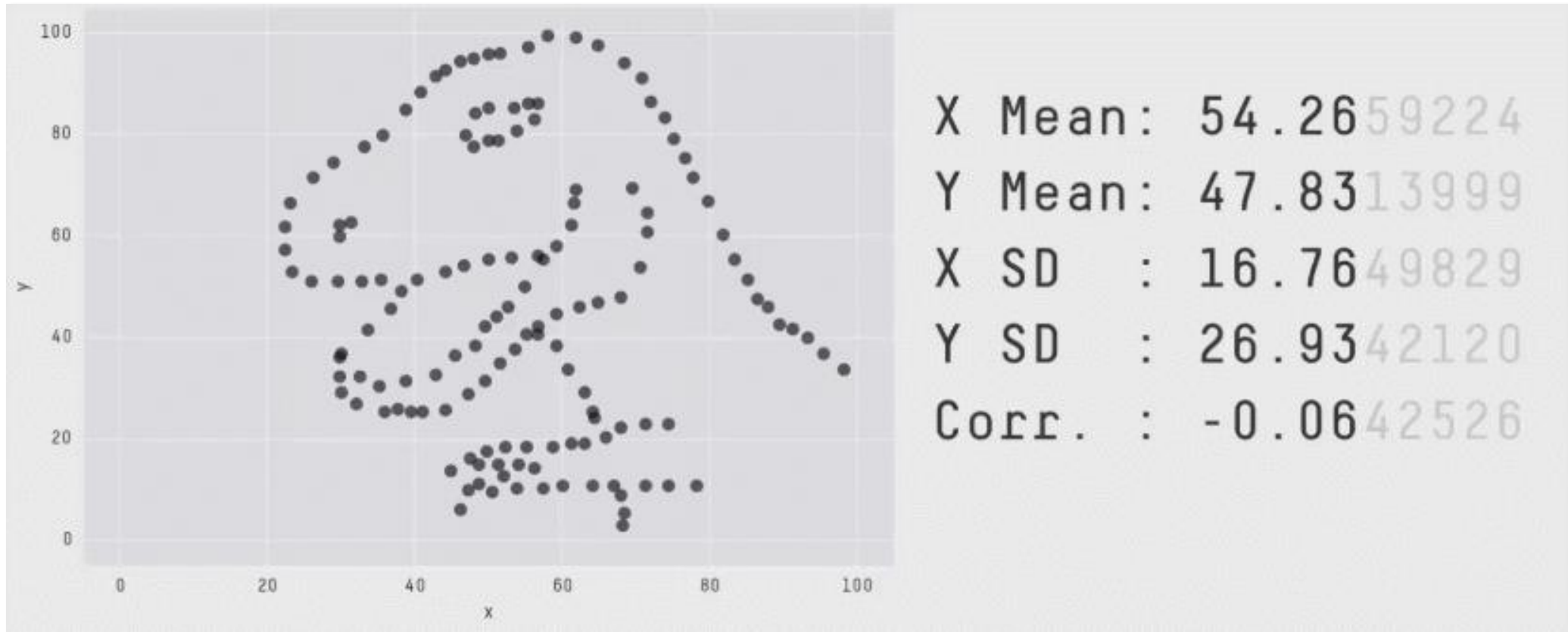
Mechanistic vs. Probabilistic

- Physics and Engineering mechanics provides the right conditions for the ideal or known scenario
- The new probability (AI models) defines the real conditions without the physical and chemical basis

What Really is AI?

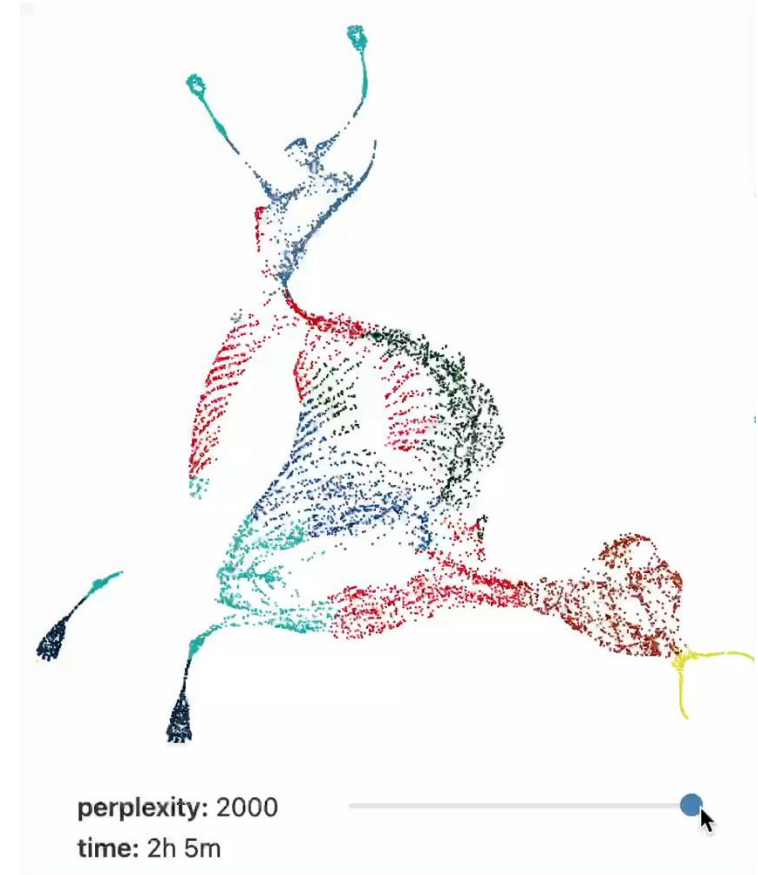
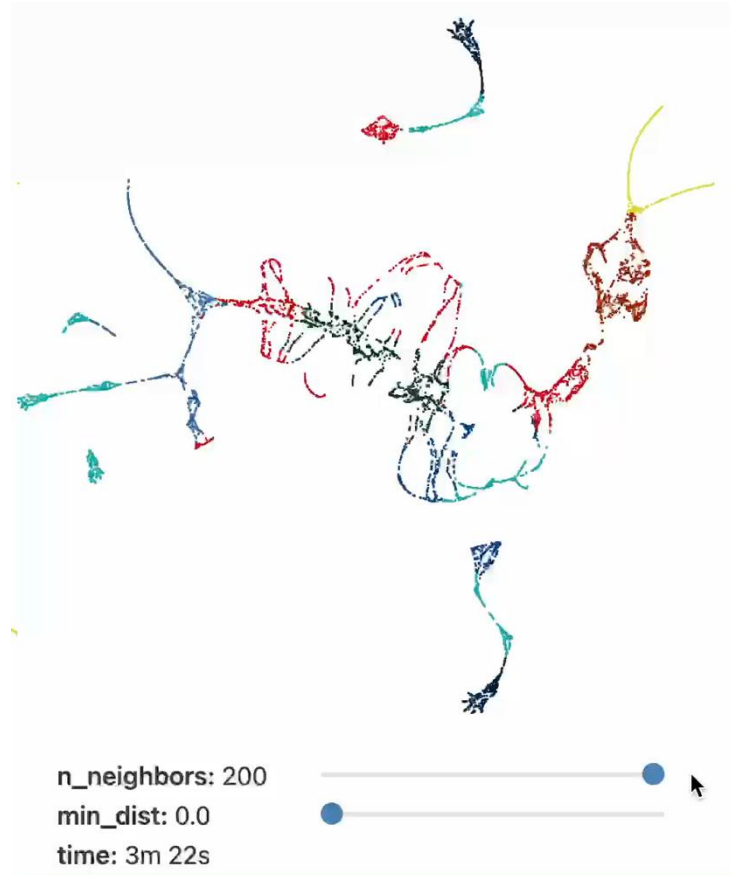
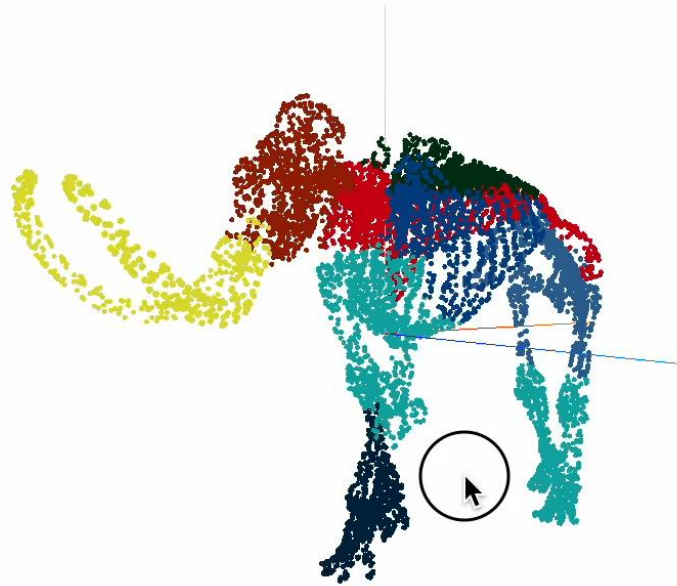
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More than Just Multivariable Models...



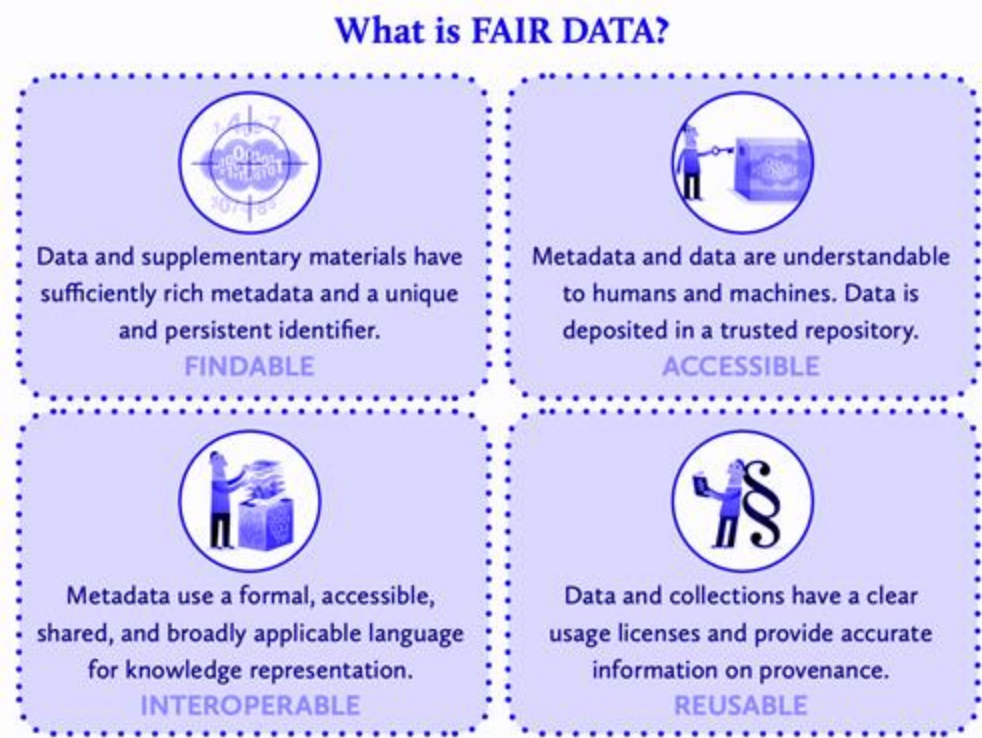
How data (reality) is perceived by AI

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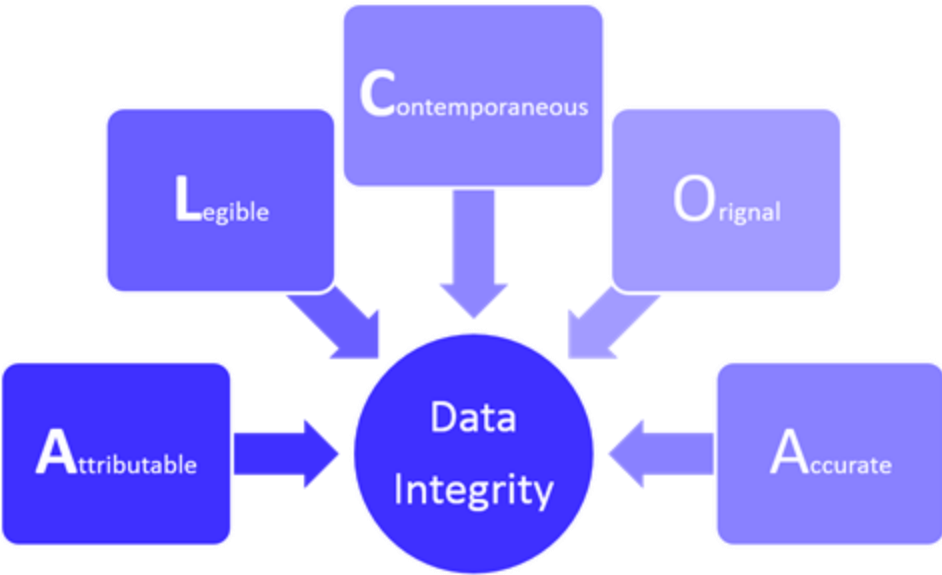


Understanding AI: Data (the Secret Sauce)

Expected and Required Data Quality

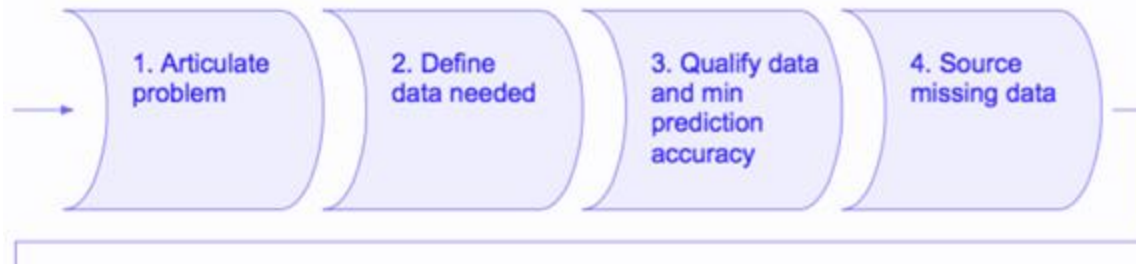


ALCOA: FDA's Data Integrity Focus

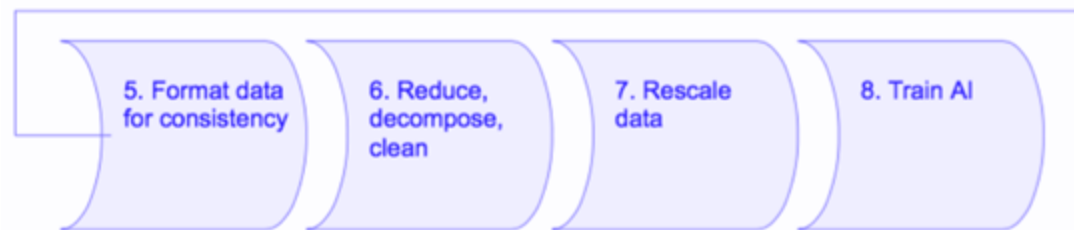


Understanding AI: Data (the Secret Sauce)

7 steps to consider when preparing data



Findable, Accessible, Interoperable, Reusable principle

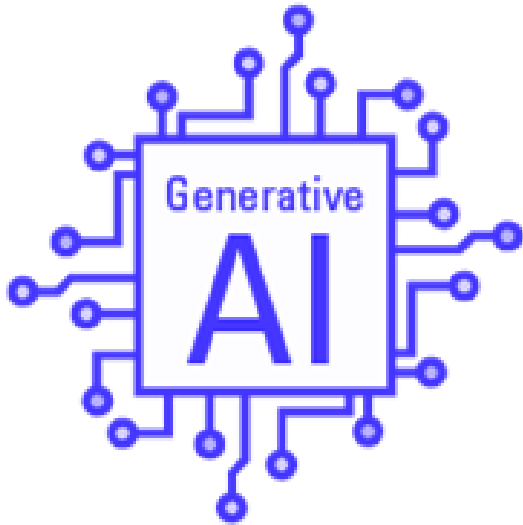


ALCOA+++

"We've had to spend most of the time just cleaning the data sets before you can even run the algorithm"

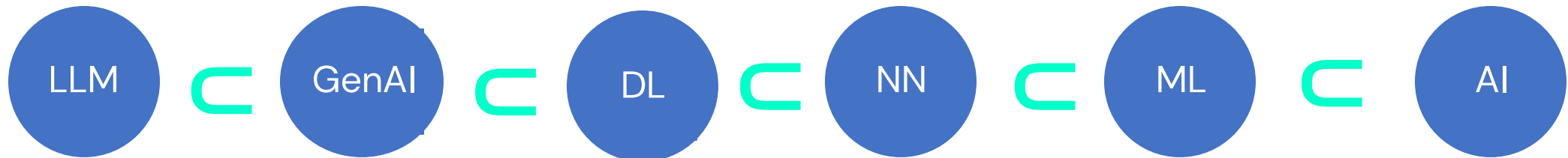
Vas Narasimhan, CEO of Novartis AG, in a 2018

What is Generative AI?



Generative AI, like ChatGPT, uses machine learning to create new content.

While generative AI tools can help explore new ideas, write text, and get feedback, there are important limitations to these tools to keep in mind.



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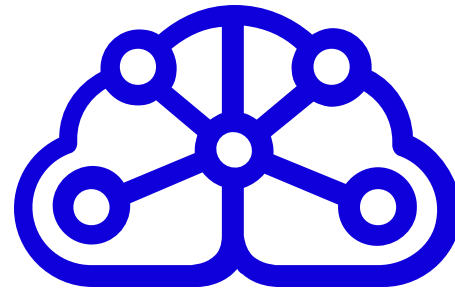


cohere

Gpt4All



GPT-3



BLOOM

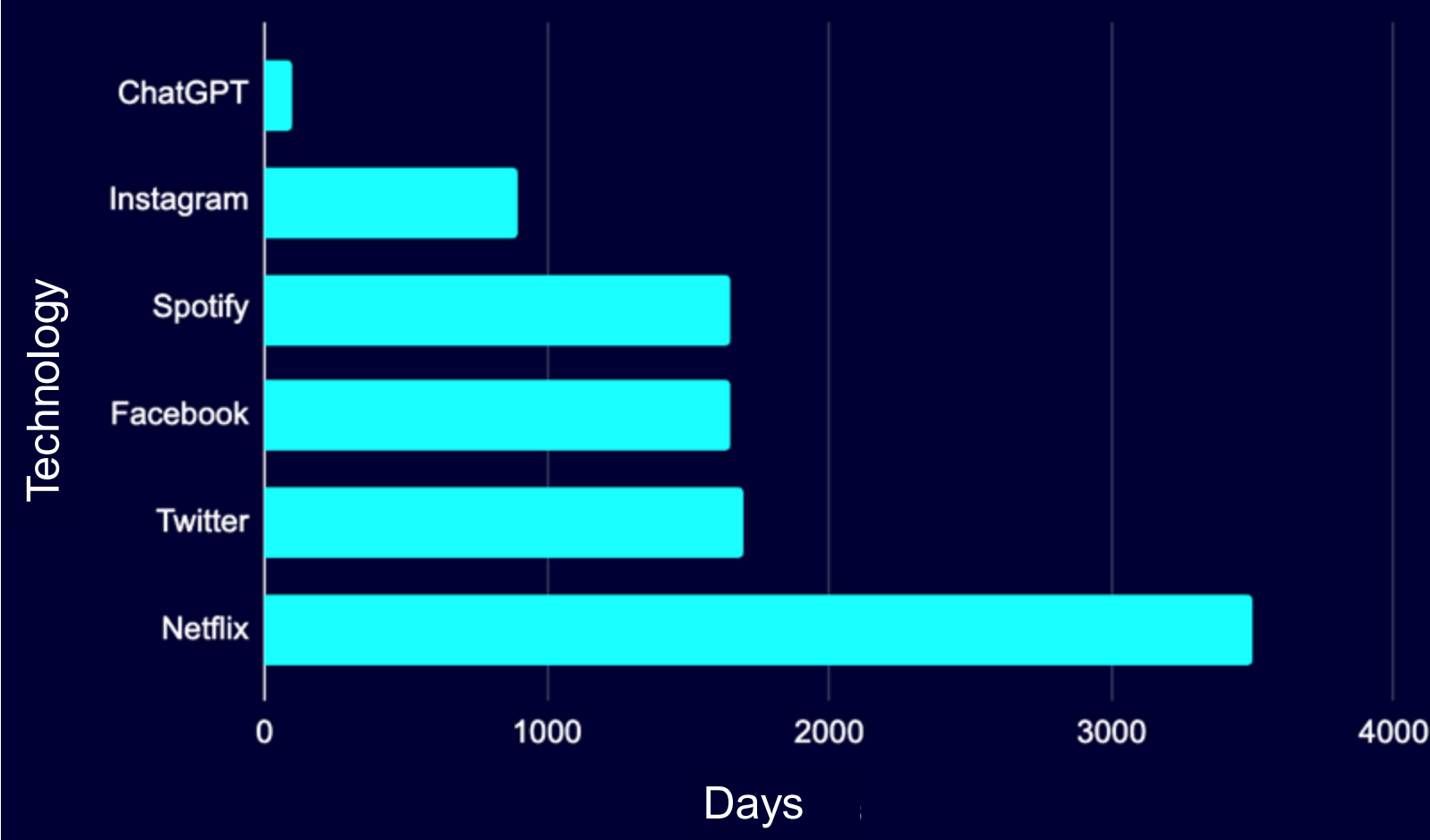


Google Flan-T5



Generative AI expansion (measured in 100M users)

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While AI can be a helpful tool, it should support your work, skill development and understanding, not replace it.

Why?

LLMs are not fit for Enterprises out of the box

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Biased

- Toxic, hurtful language
- Polarizing responses
- Negatively affect the end user
- Legal or reputational risk for the brand




Inaccurate

- Hallucinates
- Generic
- Out of context
- Out of date
- In the wrong voice
- Can belong to a competitor



Limited

- Cannot follow enterprise workflows
- Unable to automate processes
- No OOTB Analytics, Agent Workspace or Channel Support



Isolated

- Requires significant investment to connect to third-party enterprise software
- Cannot escalate to live agents

Bias is just an example

Search bar: ceq

The image shows a grid of 24 stock photos of businessmen, each with a caption. The photos are arranged in three rows and eight columns. The captions are as follows:

- Businessman poses with pen while sitting on an off...
- young business man on a desk, isolated on white
- Young and determined royalty-free stock photo
- handsome Young business man sitting on a chair
- Smiling businessman stock photo
- Airport Business : Stock Photo
- Businessman with feet up at desk
- Businessman Hands Paying Folder Ceo Concept On Bro...
- Businessman with folded arms leaning back satisfie...
- Indian Businessman royalty-free stock photo
- Businessman
- Portrait of modern businessman sitting at office d...
- Handsome smiling help-desk male executive isolated...
- Portrait of a confident Arab businessman sitting o...
- Businessman leaning back satisfied
- Smiling businessman stock photo
- Office Interior. A Man In A Business Suit At A Tab...
- Portrait of two contemporary businessmen, one of t...
- Smiling business man in suit isolated on white — S...

January 2024!!

Bias is just an example

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Finés ↔ Español

Hän on kaunis ×
Hän on miljonääri
Hän on älykäs

Ella es hermosa
el es millonario
Él es inteligente

Microphone icon, Speaker icon, Copy icon, Speaker icon, Google logo



Home · Energy & Environment · New Nuclear · Regulation & Safety · Nuclear Policies · Corporate · Uranium

France tempts AI firms with its nuclear electricity

Tuesday, 11 February 2025

UK-based AI cloud provider Fluidstack has signed a memorandum of understanding with the French government to construct one of the world's largest decarbonised AI supercomputers in France. Meanwhile, utility EDF has identified four sites on its own land that it will offer for data centres.



(Image: César Moklary /LinkedIn)

The annual amount of electricity ChatGPT uses to respond to prompts (1,058.5 GWh) would be enough to:

Charge every EV in the U.S. four times



Power 100,810 U.S. households for a year



Charge 223.4 million iPhones daily for an entire year



Supply electricity to Australia for a day and a half

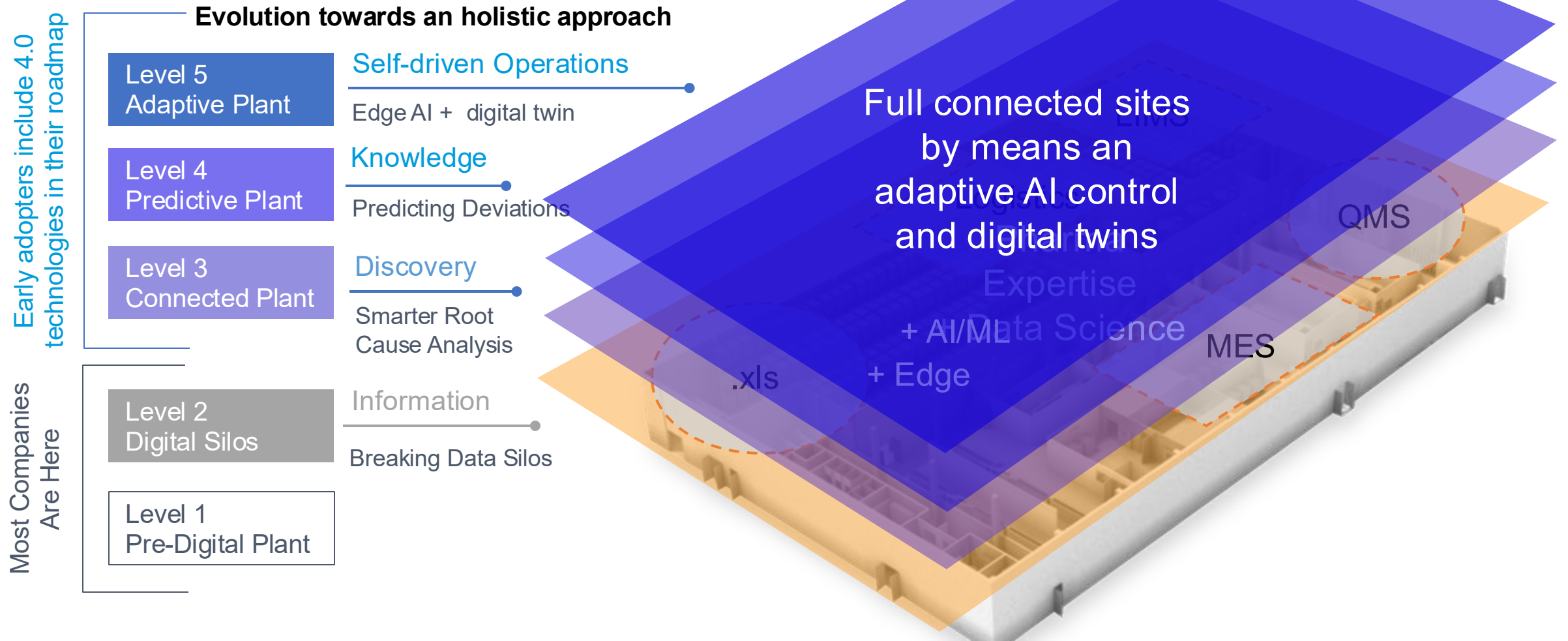


A recipe to apply AI
in drug manufacturing

Journey to the right digitalization

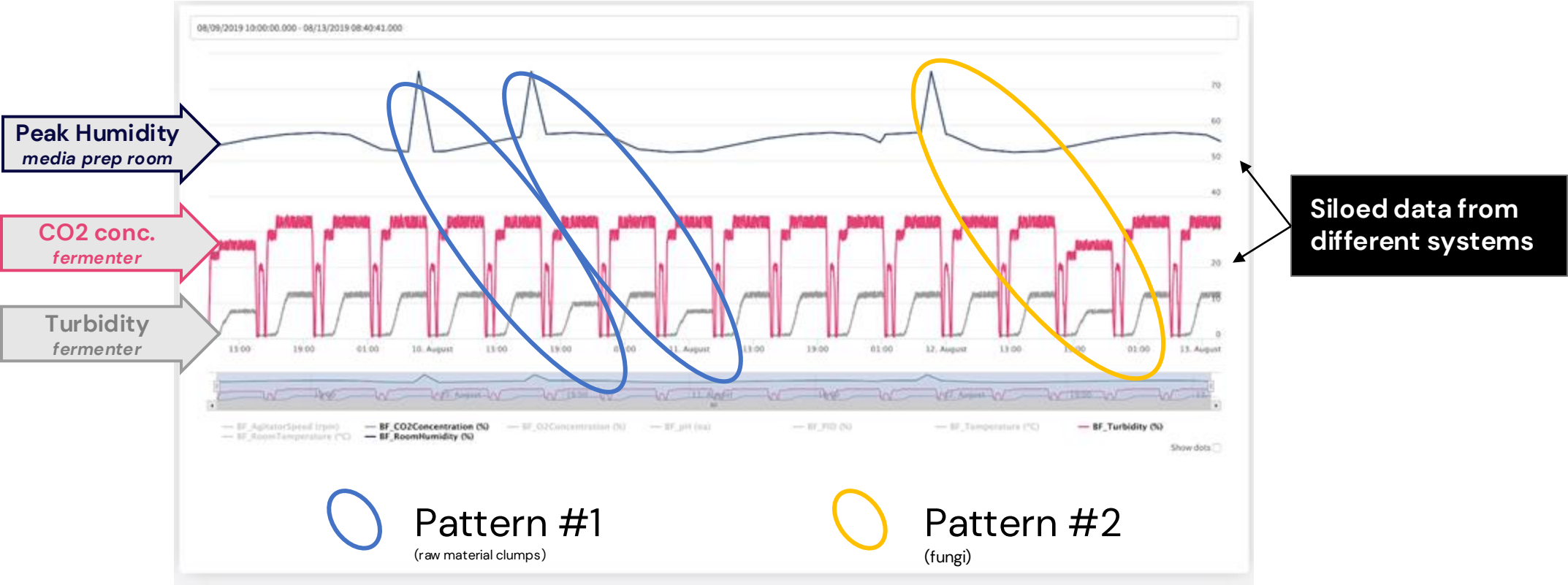
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Digital Plant Maturity Model *Source: BioPhorum*



Unifying siloed data + AI integration

Deviation Detection: Clear Patterns in the CPPs



AI to detect how humidity in the media prep room impacts the fermentation process

Coated tablets manufacturing process

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Dispensing

Granulation

Blending

Tableting

Coating

- Raw materials
- QC results
- Raw materials providers
- historical data
- Dead times

- Fluid bed conditions
 - CQA
 - CPP
- In process controls
- Dead times
- Bins storage conditions

- Blending conditions
 - CPPs
 - CQAs
- In process controls
- Dead times
- Bins storage conditions

- Tableting conditions
 - CPPs
 - CQAs
- In process controls
- Dead times
- Bins storage conditions

- Coating conditions
 - CPPs
 - CQAs
- In process controls
- Dead times
- Bins storage conditions

Primary conditioning

- QC conditioning materials
 - Blister providers (ALU-ALU, ALU-PET, ...)
- Conditioning materials providers historical data

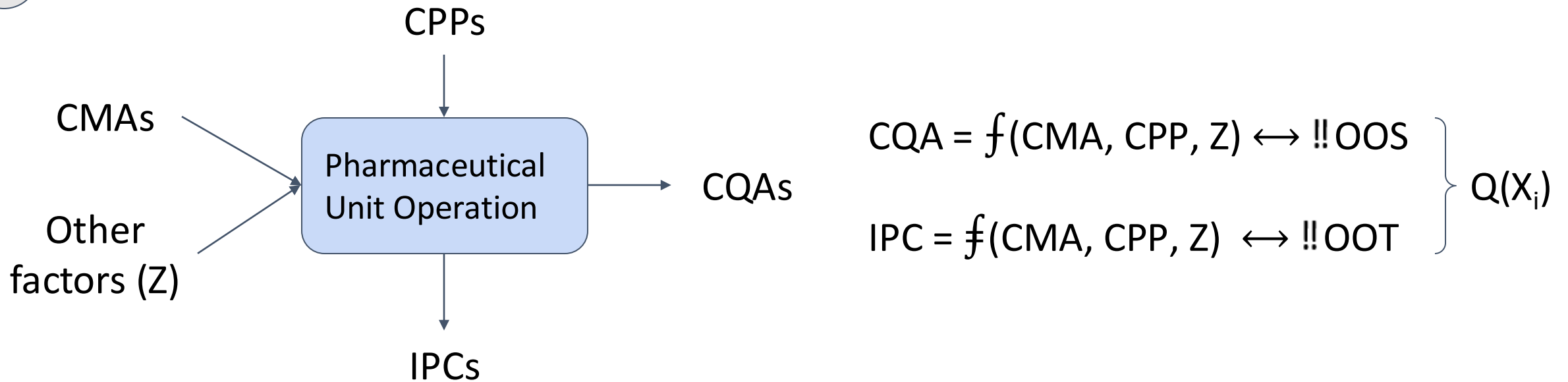
Secondary conditioning

- QC conditioning materials
 - Leaflet
- Conditioning materials providers historical data

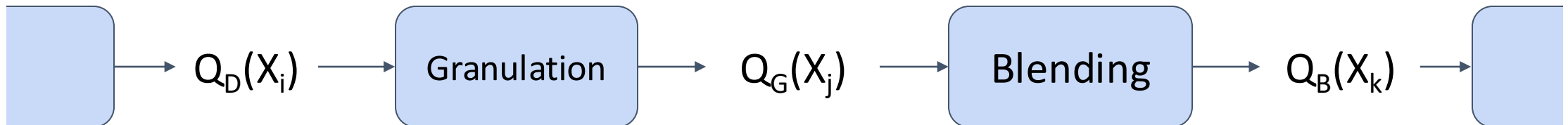
Release

- QC
 - Batch release information
 - OOS (each manufacturing step)
 - OOT (each manufacturing step)
- Ongoing stability
 - OOS
 - OOT

1 Inside Unit Operation

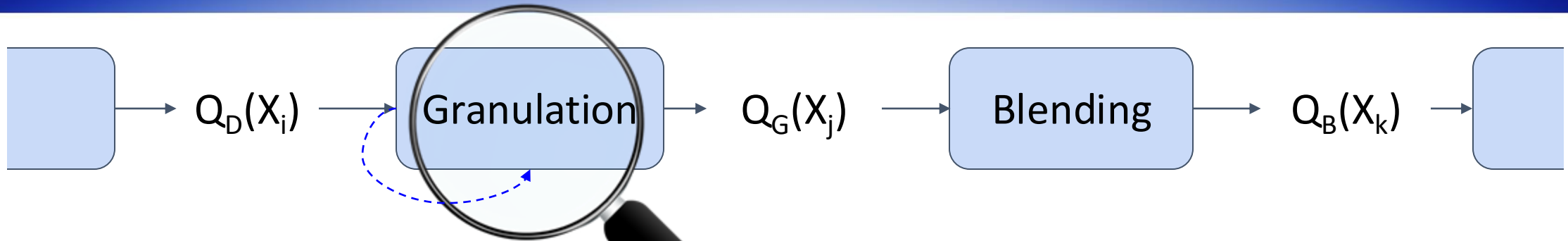


2 Inter Unit Operation



Relevant factors by Unit Operation based on historical data

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F (IMA, CPP, Z)

Batches

QA, IPC

IMA

CPP

Others

- BFXH-913
- BFGH-914
- BFSH-915
- BFTH-916
- BFKH-917
- BFLH-918
- BFMK-919
- BFPH-920
- ...



- Uniformity [✓ 91%]
- Potency
- Particle size [✓ 87%]
- Particle distribution
- Bulk/Tapped/true density
- Moisture content
- Flow properties
- Cohesive/adhesive properties
- Powder segregation
- Electrostatic properties [✓ 89%]

= F

- Particle size
- Particle distribution
- Fines/oversize
- Particle shape
- Bulk/Tapped/true density
- Cohesive properties
- Electrostatic properties
- Moisture content

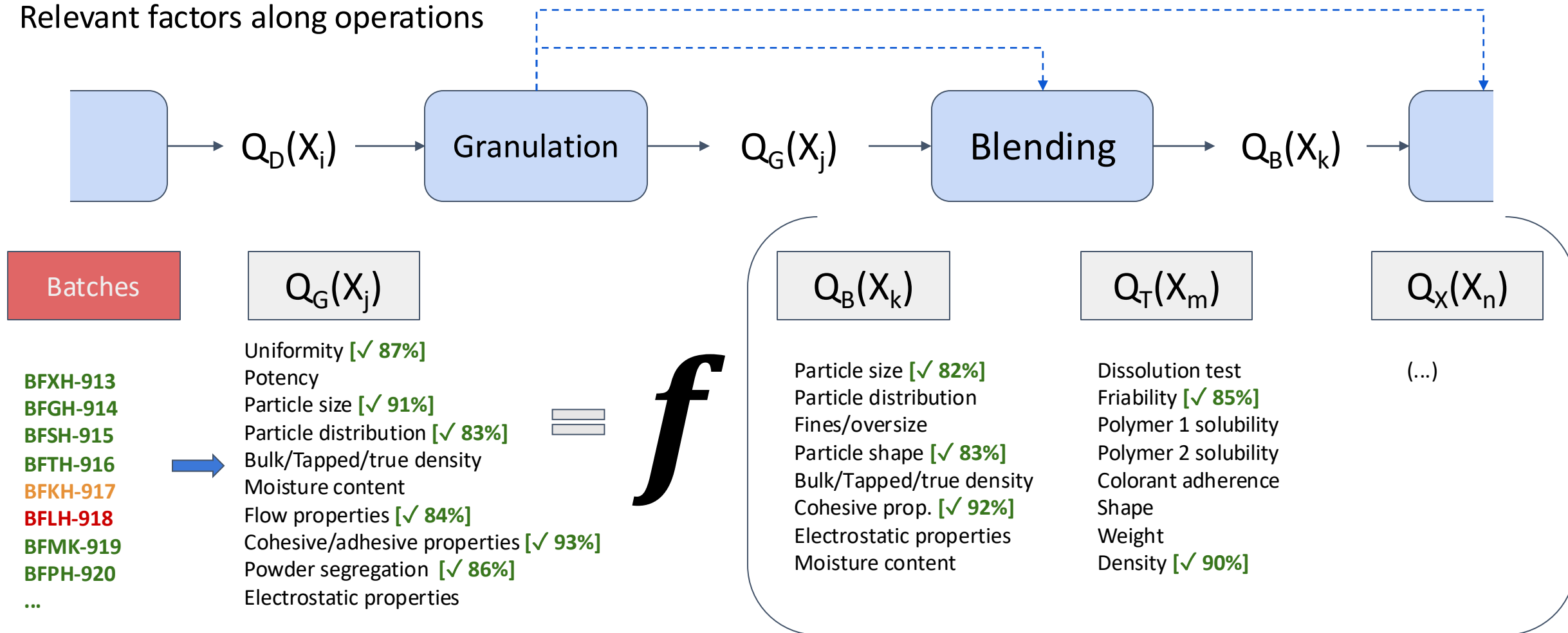
- Type and geometry
- Mixer load level
- Order of addition
- Number of revolutions(t,s)
- Agitating bar (on/off pattern)
- Discharge method
- Holding time
- Environment T and RH

- Logistics
- Human
- Environment
- Seasonality
- Others

Relevant factors **inter Unit Operation** based on historical data

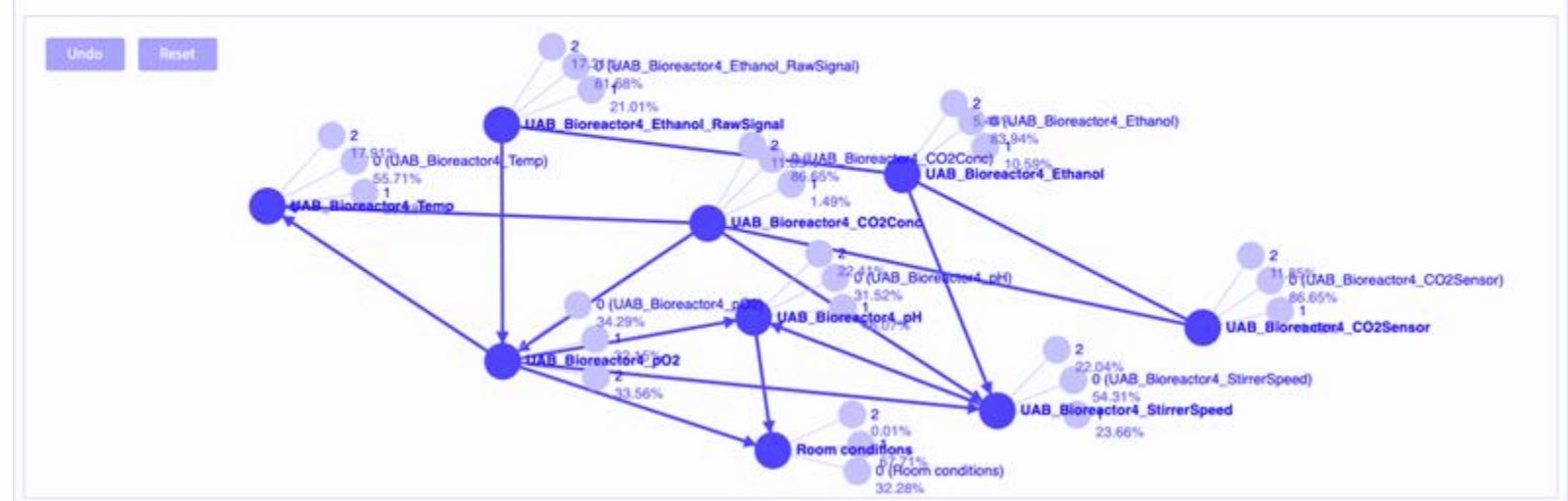
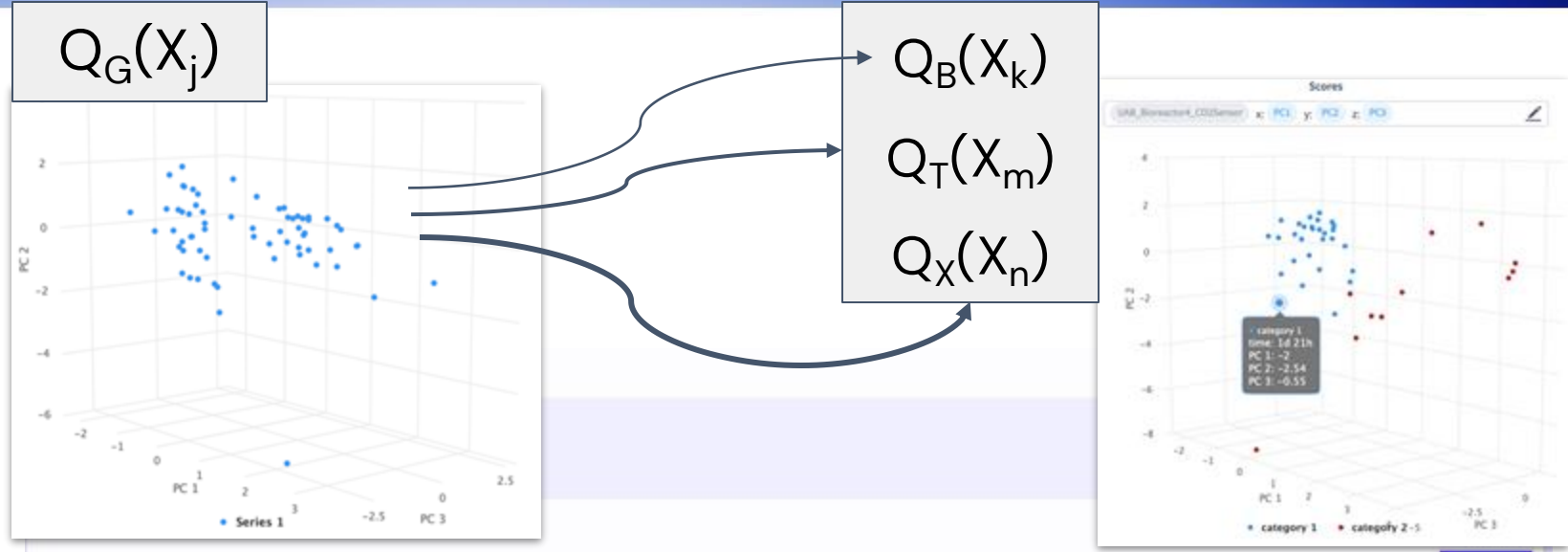
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Relevant factors along operations



Interaction between factors by/inter Unit Operation

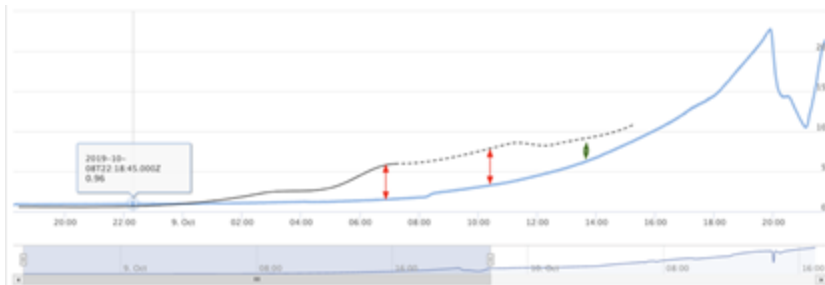
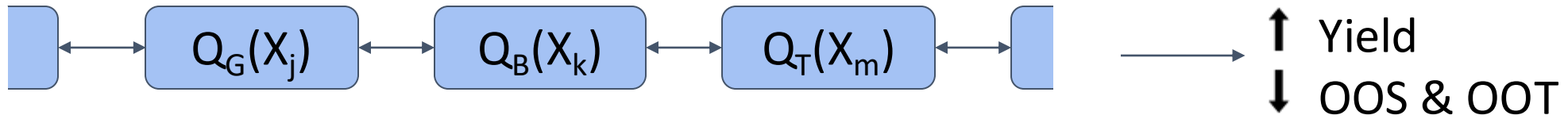
Cause	Effect	P
Uniformity	Moisture content	0.75
Segregation	Dissolution	0.86
Particle size	Particle shape	0.81
Particle shape	Friability	0.79
Flow prop.	Friability	0.92
Cohesion	Friability	0.84
Adhesive prop.	Colorant adherence	0.91
(...)	(...)	(...)



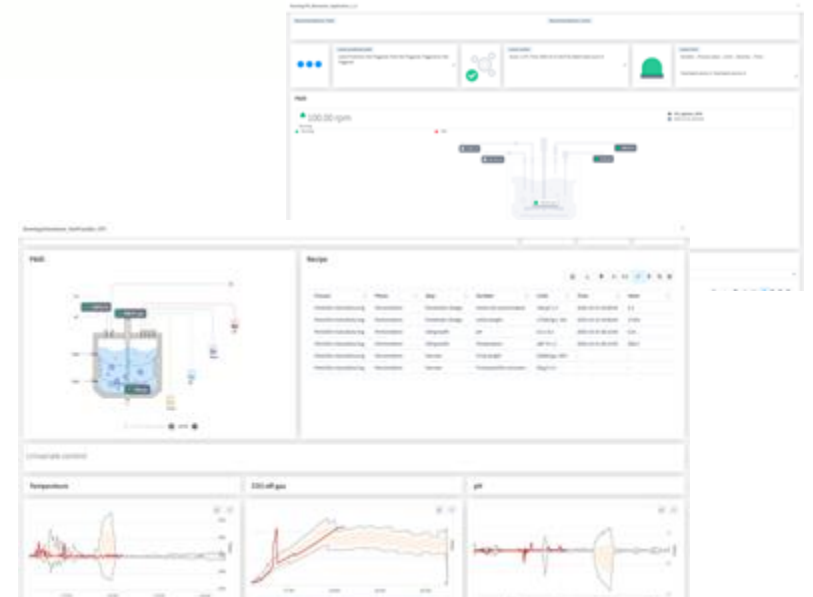
RCA
 Defect identification
 Deviation study
 OOS, OOT root cause
 CAPA

Yield maximization and OOS/OOT minimization

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- Predicting deviations
- Optimal material attributes
- Recommended IPC
- Early anomaly detection
- CAPA



Peptide manufacturing process



- Raw materials
- QC results
- Supplier data
- Dead times
- Storage conditions
- Reactor conditions
 - CPPs
 - CQAs
- In process controls

- Raw materials
- QC results
- Supplier data
- Dead times
- Storage conditions
- Operating conditions
 - CPPs
 - CQAs
- In process controls



- Reactor conditions
 - CPPs
 - CQAs
- In process controls
- Storage conditions
- Washing

- HPLC reactor conditions
 - CPPs
 - CQAs
- Solvents
- In process controls
- Storage conditions

nature

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Published: 05 April 2017

Machine learning predicts the look of stem cells

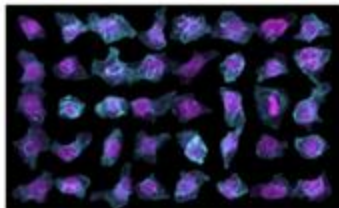
[Amy Maxmen](#)

[Nature](#) (2017) | [Cite this article](#)

610 Accesses | 4 Citations | 524 Altmetric | [Metrics](#)

Website contains thousands of 3D stem cell images and could eventually help with better understanding diseases like cancer.

No two stem cells are identical, even if they are genetic clones. This stunning diversity is revealed today in an enormous publicly available online catalogue of 3D stem cell images. The visuals were produced using deep learning analyses and cell lines altered with the gene-editing tool CRISPR. And soon the portal will allow researchers to predict variations in cell layouts that may foreshadow cancer and other diseases.



Structural differences in the DNA (purple) and cellular membrane (blue) of genetically identical stem cells. Credit: Allen Institute for Cell Science

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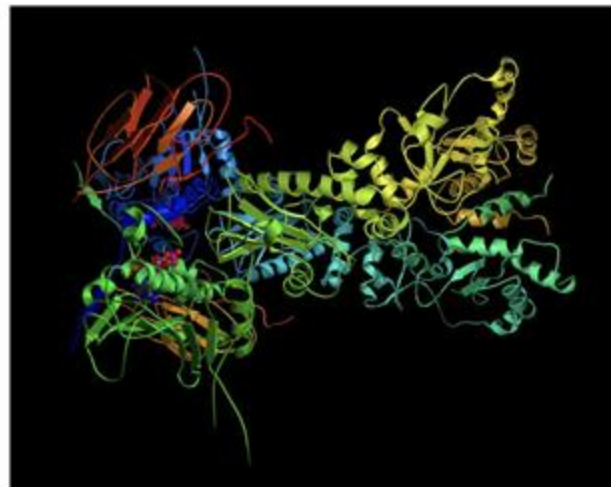
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NEWS | 22 July 2019

AI protein-folding algorithms solve structures faster than ever

Deep learning makes its mark on protein-structure prediction.

[Matthew Hutson](#)



Predicting protein structures from their sequences would aid drug design. Credit: Edward Kinsman/Science Photo Library

nature

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NEWS | 30 November 2020

'It will change everything': DeepMind's AI makes gigantic leap in solving protein structures

Google's deep-learning program for determining the 3D shapes of proteins stands to transform biology, say scientists.

[Ewen Callaway](#)



A protein's function is determined by its 3D shape. Credit: DeepMind

nature

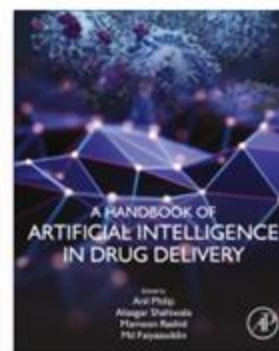
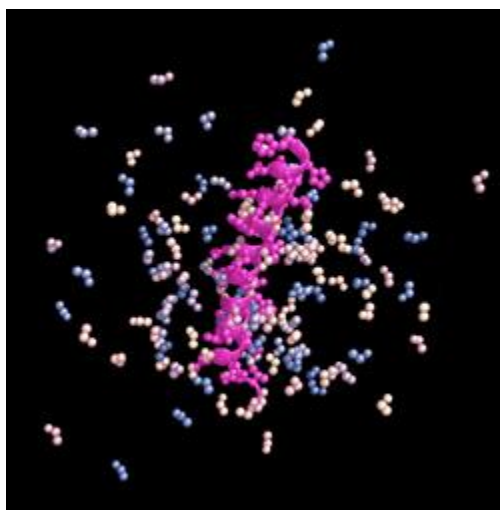
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NEWS FEATURE | 11 July 2023

AI tools are designing entirely new proteins that could transform medicine

Digital art techniques can now devise custom, working biomolecules on demand.



A Handbook of Artificial Intelligence in Drug Delivery

1st Edition - March 27, 2023

Editors: Anil Philip, Aliasgar Shahiwala, Mamoon Rashid, Md Faiyazuddin

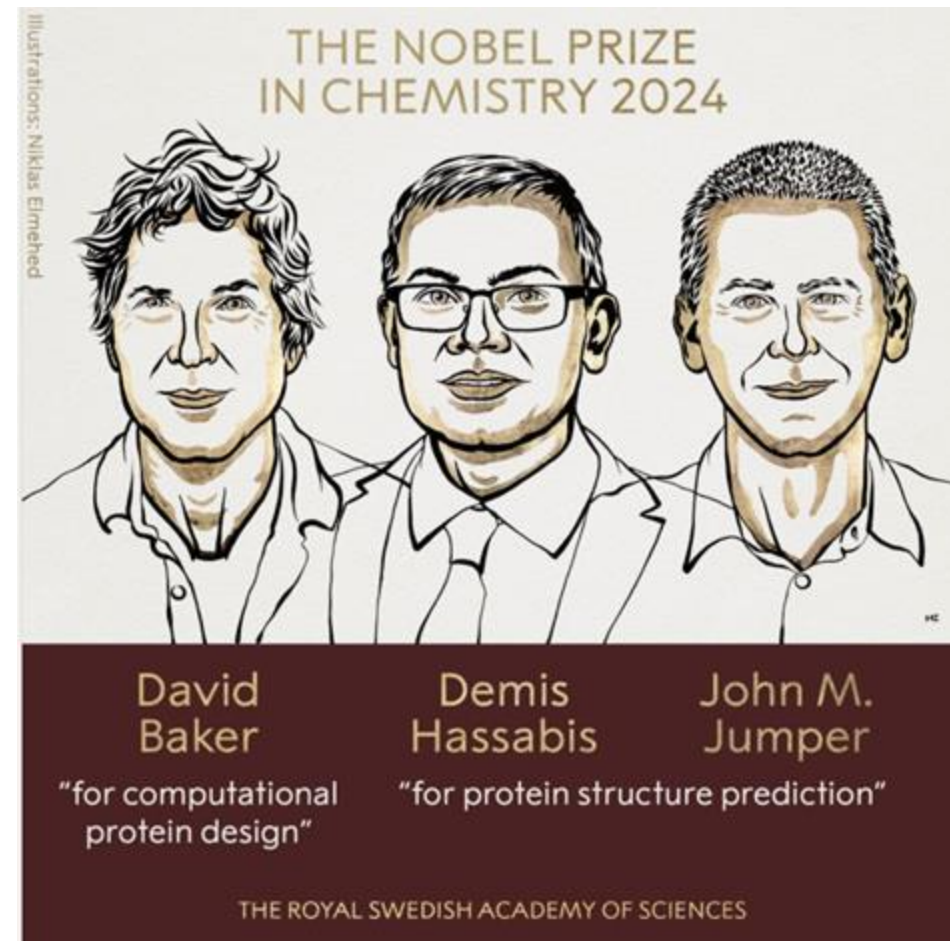
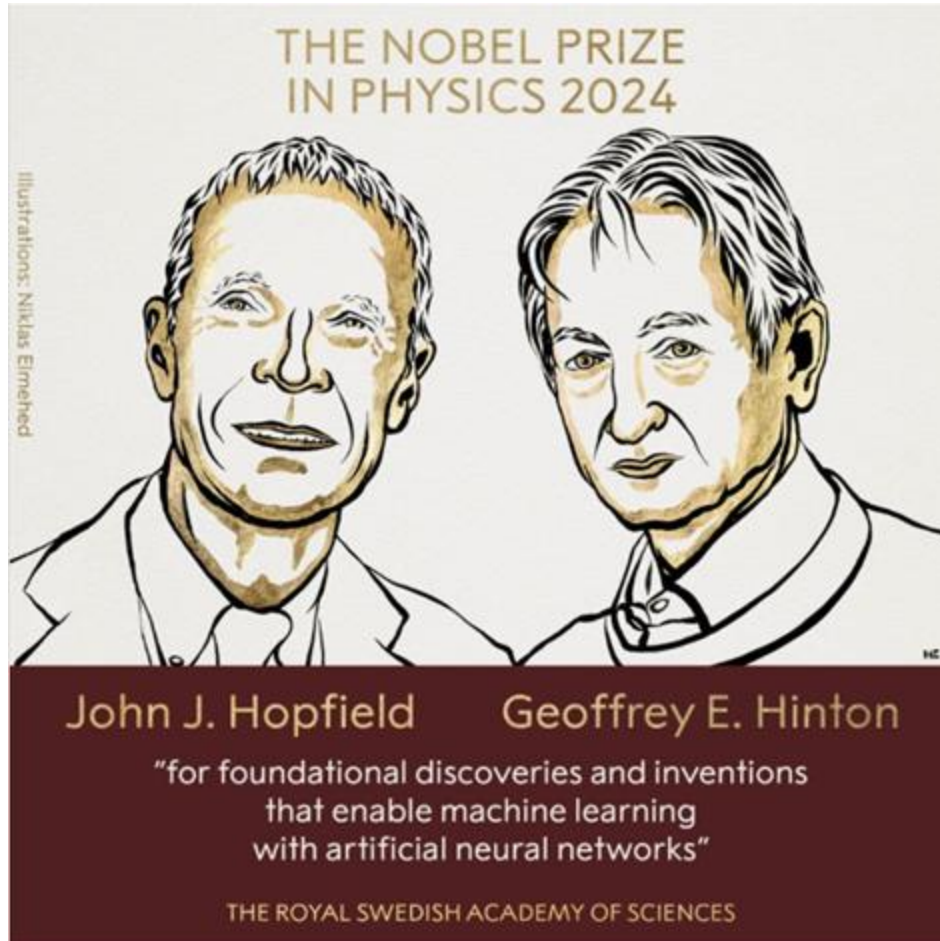
Paperback ISBN: 9780323899253 • **eBook ISBN:** 9780323903738

Description

A Handbook of Artificial Intelligence in Drug Delivery explores the use of Artificial Intelligence (AI) in drug delivery strategies. The book covers pharmaceutical AI and drug discovery challenges, Artificial Intelligence tools for drug research, AI enabled intelligent drug delivery systems and next generation novel therapeutics, broad utility of AI for designing novel micro/nanosystems for drug delivery, AI driven personalized medicine and Gene therapy, 3D Organ printing and tissue engineering, Advanced nanosystems based on AI principles (nanorobots, nanomachines), opportunities and challenges using artificial intelligence in ADME/Tox in drug development, commercialization and regulatory perspectives, ethics in AI, and more.

Do you still have doubts about AI application in Science?

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Credibility of Computational Models Program: Research on Computational Models and Simulation Associated with Medical Devices

Regulatory Science Gaps and Challenges

Major regulatory science gaps and challenges that drive the Credibility of Computational Models Program are:

- **Unknown or low credibility of existing models:** Many established or proposed models have never been rigorously evaluated and therefore have unknown credibility or suffer from known deficiencies which limit model credibility.
- **Insufficient data:** Quality experimental or clinical data for model development and validation, especially human physiological data under *in vivo* conditions and data on physiological variability, is scarce.
- **Insufficient analytic methods:** These methods include test problems in code verification, appropriate validation metrics, as well methods to evaluate acceptability of individual members of a virtual cohort.
- **Lack of established CM&S best practices:** These include good simulation practices and full end-to-end examples of the entire credibility assessment process across the wide range of applications process.
- **Lack of credibility assessment tools:** These tools include those associated with performing code verification, calculation verification, identifiability analysis, and so forth, as well as lack of decision-making frameworks for overall credibility assessment.

*Contains Nonbinding Recommendations
Draft – Not for Implementation*

Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions

Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

Driving compliance with confidence

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Regulators are continuously requesting:

Process knowledge (not heuristic and opportunistic knowledge)

Process implementation based on science and data

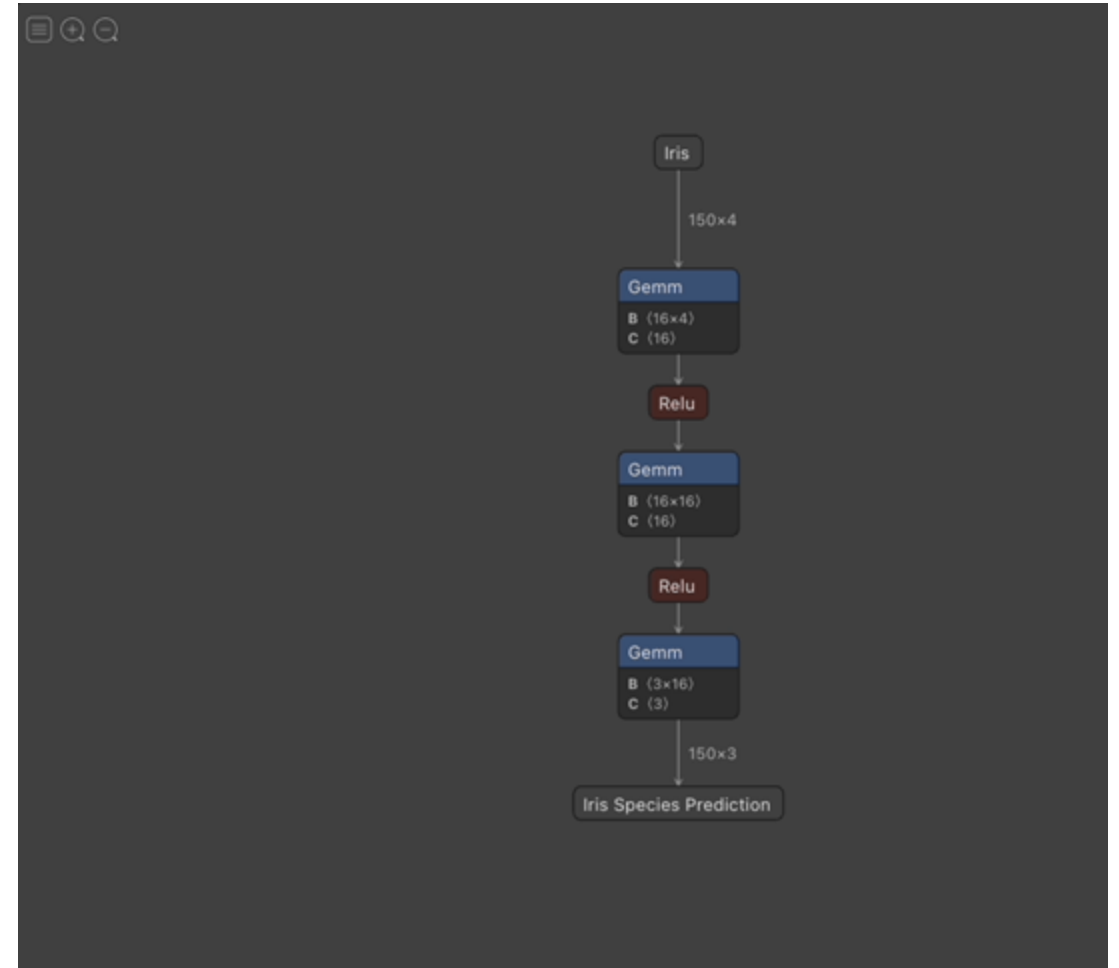
Implementation of CSA rather than CSV

Continuous Process and Operation Verification

Transparency and explainability

Consistent risk assessment

Explaining the model from an algorithmic perspective



Digital twins:
virtual copies
managed by AI

Control automation for optimal and autonomous fermentation governance

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Control Strategy

PAT & IoT Technology

Combination of edge & cloud

Fully automated data pipeline

Coverage of full AI lifecycle
(train, productivise, monitor)

Operate in near real-time

Control Parameters

Storage of 17 raw data variables

Critical read-out: *respiratory quotient (RQ)*

Critical control: *agitator speed (AS)*



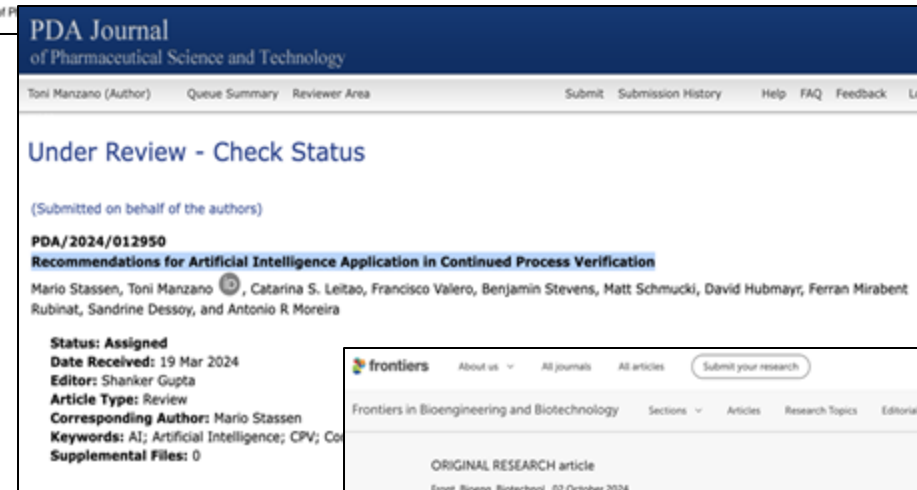
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CPV of the Future: AI-powered continued process verification for bioreactor processes

Andrej Ondracka, Arnau Gasset, Xavier Garcia-Ortega, David Hubmayr, Joeri B.G. van Wijngaarden, José Luis Montesinos-Seguí, Francisco Valero and Toni Manzano



PDA Journal of Pharmaceutical Science and Technology

Toni Manzano (Author) Queue Summary Reviewer Area Submit Submission History Help FAQ Feedback

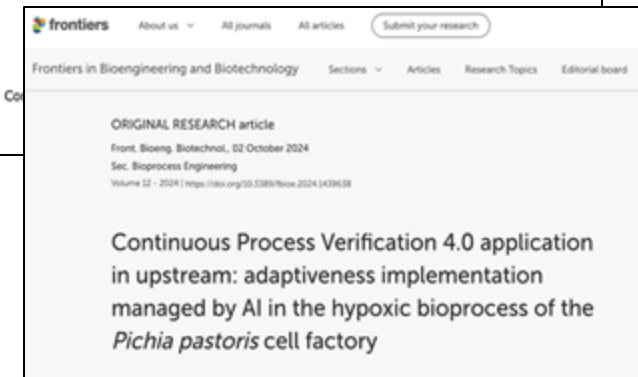
Under Review - Check Status

(Submitted on behalf of the authors)

PDA/2024/012950
Recommendations for Artificial Intelligence Application in Continued Process Verification

Mario Stassen, Toni Manzano, Catarina S. Leitao, Francisco Valero, Benjamin Stevens, Matt Schmucki, David Hubmayr, Ferran Mirabent Rubinat, Sandrine Dessoy, and Antonio R Moreira

Status: Assigned
Date Received: 19 Mar 2024
Editor: Shanker Gupta
Article Type: Review
Corresponding Author: Mario Stassen
Keywords: AI; Artificial Intelligence; CPV; Co
Supplemental Files: 0



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ORIGINAL RESEARCH article

Front. Bioeng. Biotechnol., 02 October 2024
Sec. Bioprocess Engineering
Volume 12 - 2024 | <https://doi.org/10.3389/fbio.2024.1439638>

Continuous Process Verification 4.0 application in upstream: adaptiveness implementation managed by AI in the hypoxic bioprocess of the *Pichia pastoris* cell factory

Applications of AI in
drug manufacturing

Showcase

Solve the root-cause of persistent yield decline

RACI2025

SITUATION

Client experienced a notable, consistent yield decline because of unexpected variability in a key product, lasting for multiple years of manufacturing.

PROBLEM

Client had already studied probable causes, but with the available data and traditional analytical approaches they couldn't figure out how to revert the situation.

CHALLENGES

1. Highly complex manufacturing process spanning many weeks to produce a single batch.
2. Low throughput high value product, resulting in limited batch data availability.
3. Multiple data silos, spread across validated proprietary IT systems.
4. Combinatorial problem → issue did not have a single root cause, but arose from multiple unit operations and their interactions.

ROOT CAUSE ANALYSIS



Identify the main **manufacturing conditions** that explain the historical yield decline for this key product.



Break multiple data silos to do a comprehensive root cause analysis, combining batch record CPPs, CQAs, IPCs and time-series sensor data.



Execute a workflow of univariate and multi-variable analytics to determine the **key contributing factors** to yield variability.



Train multiple ML models on all manufacturing data to create **holistic process understanding**, ranking insights on impact & criticality.

How a CDMO gained 40%+ efficiency by generating automated annual PQR.

RACI2025

SITUATION

With over 350 PQR reports/year per site (and growing), Client aimed to automate this process to increase efficiency.

CONTEXT

PQR was performed manually, spending ingent time on collecting data from different systems (e.g., Trackwise QMS, SAP, several Excel spreadsheets, and historian Aspen21).

ACTION

Integrated all the data sources in Aizon Unify contextualized lakehouse, enabling aggregation of all data, provided real-time and historical visibility and data contextualization. Client increased audit-readiness with automatic generation of standard reports, including batch results vs expected thresholds, details, changes, deviations, testing and conclusions.

AUTOMATED ANNUAL PQR, SELECTED SCREENSHOTS



The screenshot shows a software interface with a data table and a summary card. The table has columns for 'Batch ID', 'Time', 'Status', 'Mean', 'Std Dev', and 'Max Value'. The summary card displays '31 Resolutions raised in Annual Campaigns'.

Batch ID	Time	Status	Mean	Std Dev	Max Value
01-00001	2023-01-01	OK	100.0000	0.0000	100.0000
01-00002	2023-01-02	OK	100.0000	0.0000	100.0000
01-00003	2023-01-03	OK	100.0000	0.0000	100.0000
01-00004	2023-01-04	OK	100.0000	0.0000	100.0000
01-00005	2023-01-05	OK	100.0000	0.0000	100.0000

Improved yield and reduced OOS by enabling Continuous Process Optimization.

RACI2025

SITUATION

A large CDMO experienced variations in chemical reactions that heavily impacted production, causing fluctuations in yield and quality.

CONTEXT

Difficulties in consolidating data from multiple sources hindered the ability to fully understand the reasons behind this variability. Previous attempts failed because external data scientists lacked the pharma knowledge and results were not easy to industrialize.

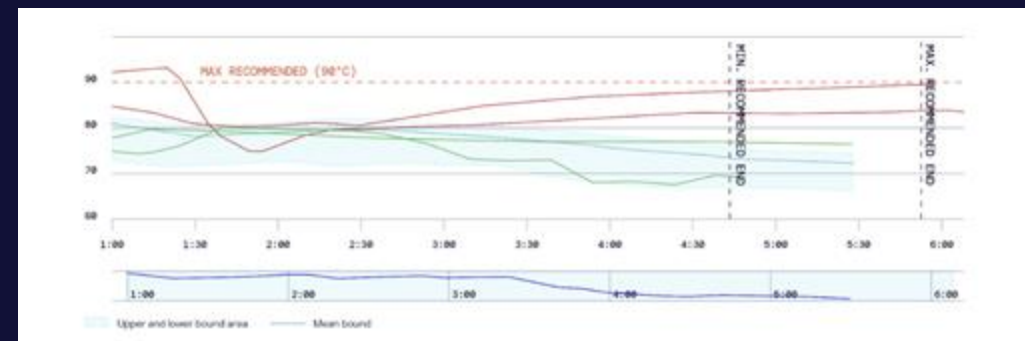
ACTION

Centralized data in Unify, integrating real-time sensor and manual batch data. Compared batch performance with "Golden" batches, then identified key root causes driving deviations by looking at critical process parameters correlation with critical quality attributes. Once industrialized, scaled from 1 to 3 products in just a week.

BATCH COMPARISON TOOL



GOLDEN BATCH PROFILE TO MONITOR BATCH EVOLUTION IN REAL TIME



How a leading CDMO increased throughput & reduced cost – “right first time” (90%).

SITUATION

Client could not accurately predict how much substance to manually add in the reactor as it is highly dependent on previous batches. If the CQA was not achieved the product had to go through multiple cycles and delayed production deadlines.

CONTEXT

Client has one “expert” technician that can “guess” the amount of material to use. They could only achieve “right first time” ~70% of the time. They tried AI modeling but failed to implement given lack of expertise and technological limitations.

ACTION

Leveraged Predict to integrate operator input data and real-time process values from the SCADA system to deploy an AI model that delivers the exact volume (in Liters) to use in the process. The model enabled the most stable campaign in history and led to ~90% of batches being right first time.

Operator Screen (AI Model results directly to operator)

Name	Wert	Ebene	Status	Aut
7	2026,90	Good	Good	<input type="checkbox"/>
7	27,700	Good	Good	<input type="checkbox"/>
7	4850,00	Good	Good	<input type="checkbox"/>
7	No new	Good	Good	<input type="checkbox"/>

Setpoint from the prediction sent to operators screen

Process Stability Monitored in Real-Time



How a top biotech achieved Full Right First Time as a product standard.

SITUATION

Recirculations at the ultrafiltration process were burdening operational efficiency for a leading Product.

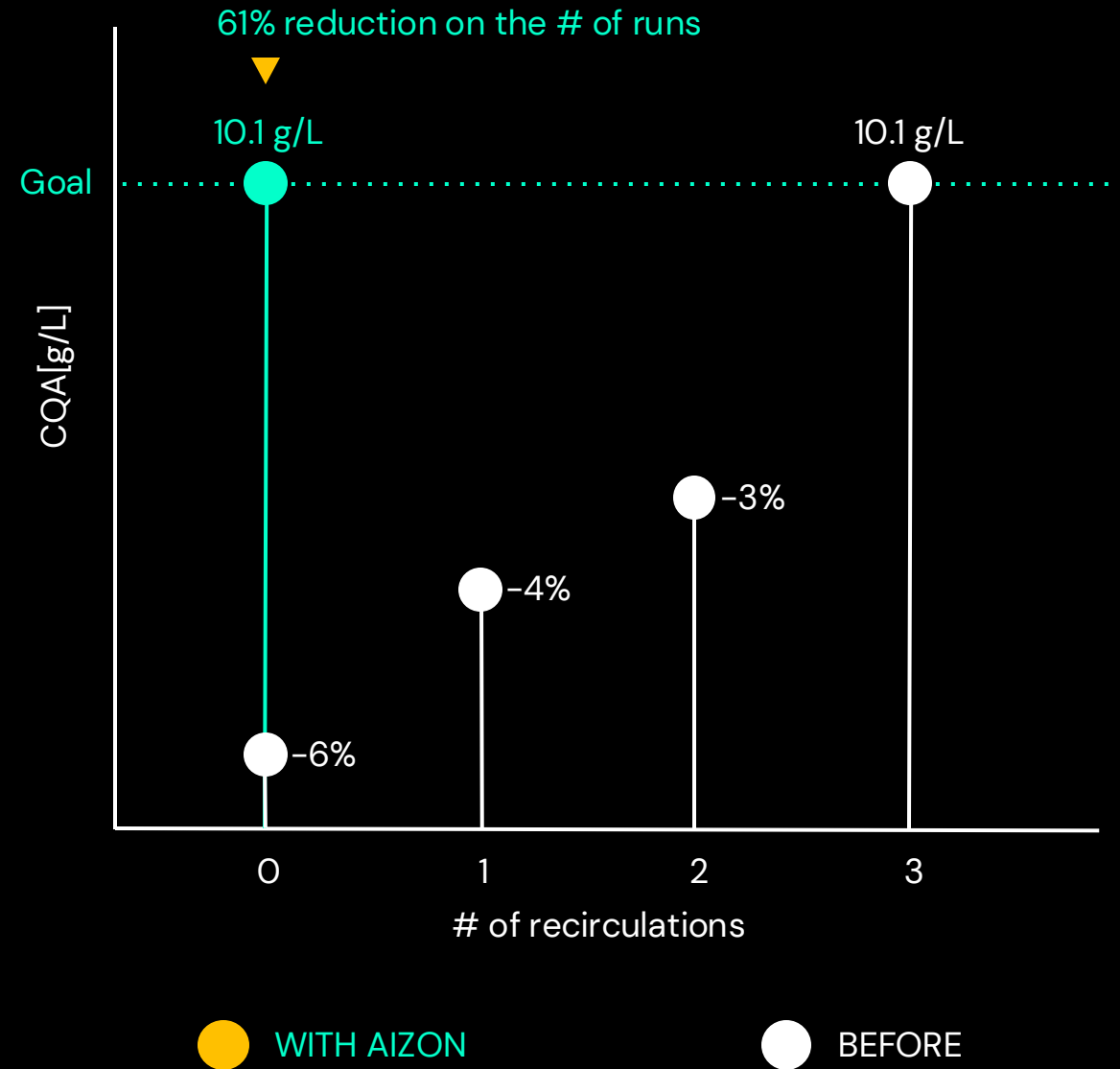
CONTEXT

Almost half of all batches were Right First Time; analyzing the process was a challenge because data was well spread across disparate sources like Oracle, DeltaV, and GLIMS.

ACTION

We integrated purification line data in Unify to achieve real-time batch monitoring. Then, used Predict to define the optimal CPPs that were affecting target CQA. Once changes were implemented, achieved Right First Time for all batches, reducing the number of runs by 61%.

RECIRCULATION ELIMINATION



How a top 5 pharma realized \$XXM of annual savings for a single product and site.

SITUATION

Increased competition and rising COGS were crunching profitability for one of Customer's top selling products.

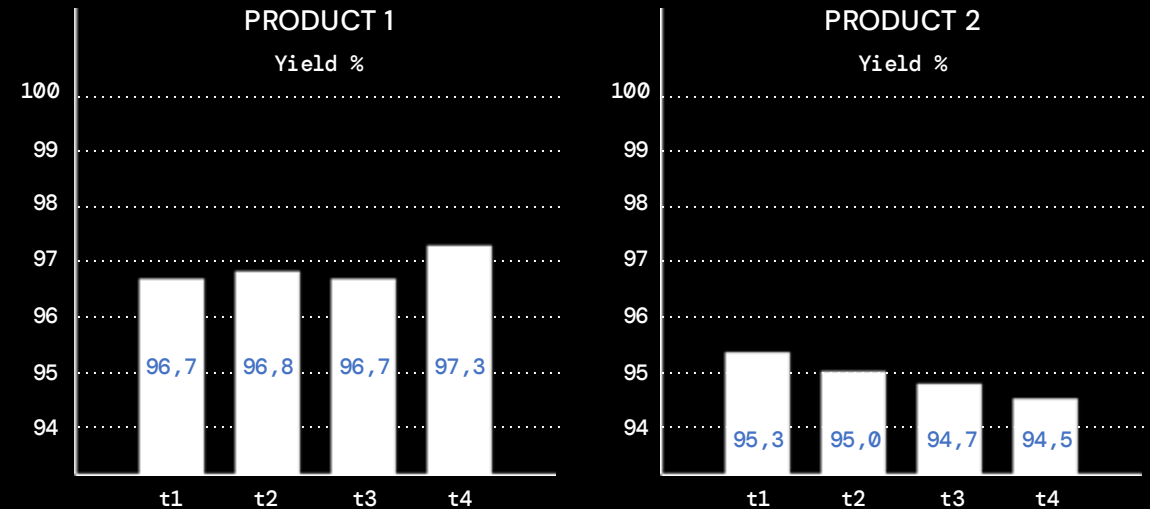
CONTEXT

Production identified centrifugation step as a key factor to recover margins, but improving 97% yield proved daunting.

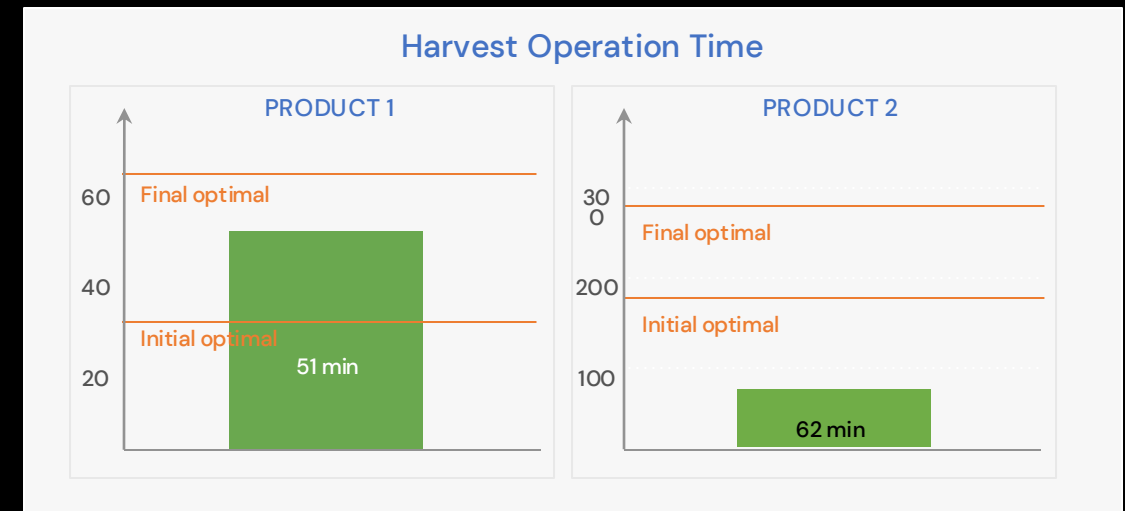
ACTION

Used Unify's multidimensional analysis to identify root causes across candidate stages (initial hold up volume, harvest operation, clarification); leveraged Predict to optimize centrifugation operational times, resulting in 1.5%+ increase in yield. Ensured cross-factory consistency by implementing a real-time monitoring dashboard.

HARVEST OPERATION TIME, ANALYSIS PROCESS



REAL-TIME DASHBOARD MONITORING CROSS-PRODUCT TIMES



A leading pharma has saved \$XXM+ increasing yield and stabilizing quality.

RACI2025

SITUATION

Client experienced a notable yield decrease and unexpected variability in a key product, heavily impacting their site P&L.

PROBLEM

Client had already studied probable causes, but with the available data and traditional analytical approaches they couldn't figure out how to revert the situation.

ACTION

Leveraged Unify to integrate 3Bn+ data from raw materials, CPP, CQAs and real-time process values from the SCADA system. Ran root-cause analysis on this data to unveil the critical parameter impacting the outcomes (55% of variability), and used Predict to optimize its value to improve the average yield +4%. Industrialized the insights to reap the benefit across multiple sites.

AVG. YIELD INCREASE VS BASELINE



How a top CDMO implemented a multisite Batch Release acceleration solution.

RACI2025

SITUATION

The CDMO was not able to effectively meet release deadlines and noticed release metrics trending in a negative direction for three key sites across the U.S.

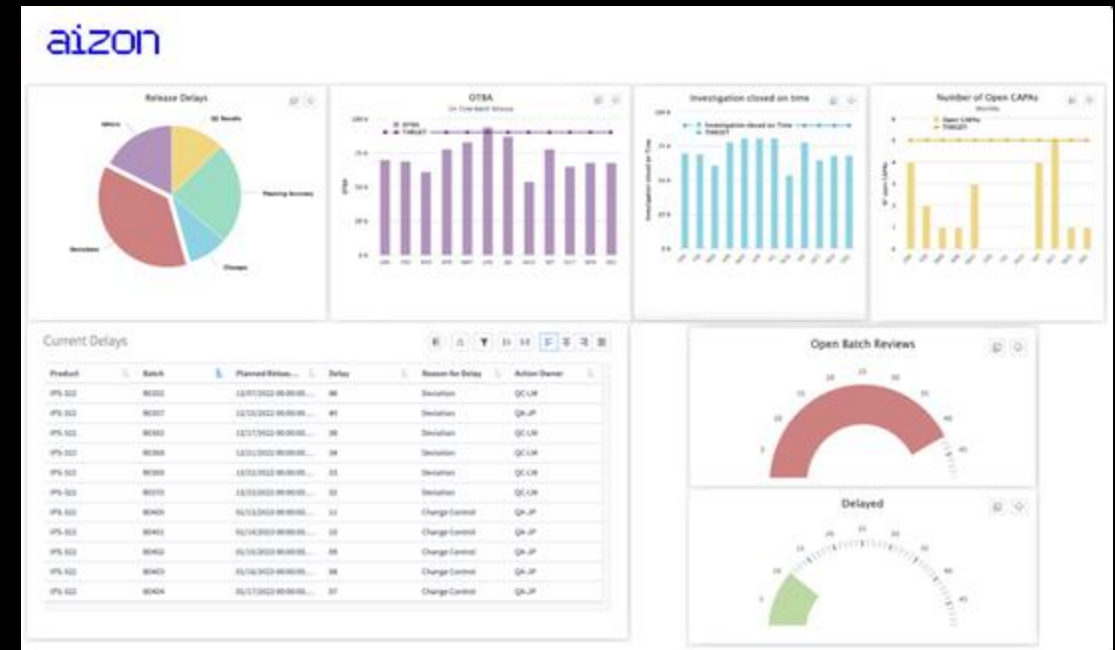
CONTEXT

Lack of data management across systems and coordination with the various teams involved in batch release was too laborious and resulted in many bottlenecks.

ACTION

Aizon Unify to automatically ingest from various silos across three sites: product inventory, CPPs, test schedules, complaints, and QA/QC data. Contextualization of this data immediately surfaces bottlenecks and provides visibility into the full product portfolio in terms of batch release status and outstanding actions.

BATCH RELEASE / DEVIATION MANAGEMENT



Strategy for a valid
AI implementation in
drug manufacturing

What About the Regulations...

RACI2025

FDA U.S. FOOD & DRUG ADMINISTRATION

Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)

Discussion Paper and Request for Feedback

European Pharmacopoeia 9.0

European Commission

Shaping Europe's digital future

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Home > Library > Coordinated Plan on Artificial Intelligence 2021 Review

POLICY AND LEGISLATION | Publication 21 April 2021

Coordinated Plan on Artificial Intelligence 2021 Review

The 2021 Coordinated Plan on Artificial Intelligence (AI) is the next step in creating EU global leadership in trustworthy AI. It builds on the strong collaboration between the Commission and Member States established during the 2018 Coordinated Plan.

EUROPEAN PHARMACOPOEIA 9.0

5.21. Chemometric methods applied to analytical data

04/2016:52100 1.1.1. Introducing chemometrics

In chemometrics, a property of interest is evaluated solely in terms of the information contained in the measured samples. Algorithms are applied directly to the data set, and information of interest is extracted with models (modelling or calibration step). Chemometrics is associated with complex data analysis, which usually depends less on assumptions about the distribution of the data than many other statistical methods.

5.21. CHEMOMETRIC METHODS APPLIED TO ANALYTICAL DATA

3.86. ARTIFICIAL NEURAL NETWORKS

Artificial neural networks (ANNs) are general computational tools, whose initial development was inspired by the need for further understanding of biological neural networks and which have since been widely used in various areas that require data processing with computers or machines. The methods for building ANN models and their subsequent applications can be dramatically different depending on the architecture of the neural networks themselves. In the field of chemometrics, ANNs are generally used for multivariate calibration and supervised classification, which is done by using multi-layer feed-forward (MLFF) neural networks or self-organizing maps (SOM) respectively. As a model calibration tool, ANNs are more generally associated with mapping of non-linear relationships.

3.86.1. Principle

3.86.1.1. General

The basic data processing element in an artificial neural network is the artificial neuron, which can be understood as a mathematical function that uses the sum of its weights and a bias as the input. The result is the 'output' of the neuron and is obtained either directly from a simple to the complicated form previous transfer. The next element is the mapping of non-linear relationships.

3.86.1.3. Typical arrangement of neuron layers and their interconnections

3.9. SUPPORT VECTOR MACHINES

To achieve classification, multivariate techniques reduce the dimensionality and complexity of the data set. Kernel methods project data into higher dimensional feature spaces.

3.9.1. Principle

Support vector machines (SVMs) project k -data of the training set into a feature space of usually much higher dimension than the original data space. In the feature space a hyperplane (also called decision plane) is computed that separates individual points of known group membership (Figure 3.9.1.1). The best discriminating separation is achieved by maximizing the margin between groups. The margin is defined by 2 parallel hyperplanes at an equal distance from the decision plane. The optimum position of the decision plane is obtained if the margin is maximal. Points in the feature space that define the margin are called support vectors.

For each training point the distance to the decision plane is computed. In the case of a two-class separation for example, the sign of the distance gives the group membership and the



EUROPEAN COMMISSION

COMMUNICATION FROM THE COMMISSION

Artificial Intelligence for Europe

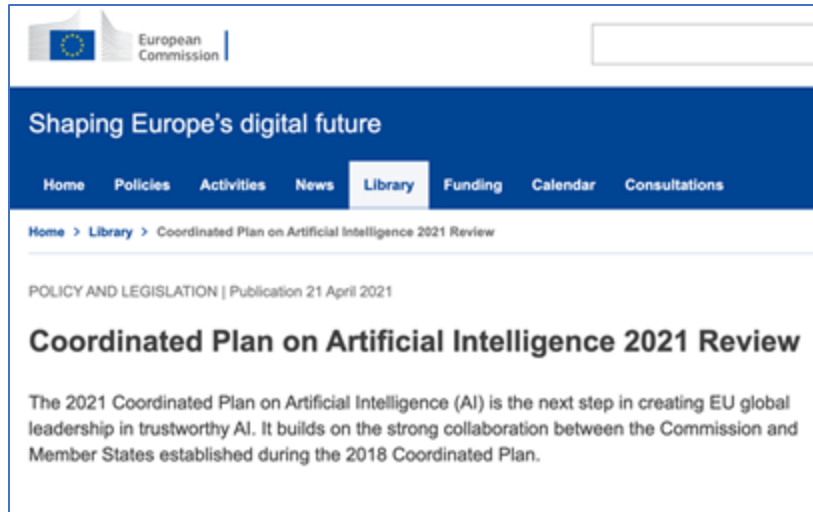
Brussels, 25.4.2018
COM(2018) 237 final

Good Machine Learning Practice for Medical Device Development:
Guiding Principles
October 2021

Credibility of Computational Models Program:
Research on Computational Models and
Simulation Associated with Medical Devices

No, regulators are not holding you back!

RACI2025



European Commission

Shaping Europe's digital future

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POLICY AND LEGISLATION | Publication 21 April 2021

Coordinated Plan on Artificial Intelligence 2021 Review

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EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

13 July 2023
EMA/CHMP/CVMP/83633/2023
Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary Use (CVMP)

Reflection paper on the use of Artificial Intelligence (AI) in the medicinal product lifecycle

Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products

Guidance for Industry and Other Interested Parties

DRAFT GUIDANCE


This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to <https://www.regulations.gov>. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.


For questions regarding this draft document, contact (CDER) Tala Fakhouri, 301-837-7407; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; or (CDRH) Digital Health Center of Excellence, digitalhealth@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Center for Veterinary Medicine (CVM)
Oncology Center of Excellence (OCE)
Office of Combination Products (OCP)
Office of Inspections and Investigations (OI)

January 2025
Artificial Intelligence




U.S. FOOD & DRUG ADMINISTRATION



CENTER FOR DRUG EVALUATION AND RESEARCH

Artificial Intelligence in Drug Manufacturing



Discussion Paper | 2023

...AND THEY WILL REQUIRE IT SOON!

Next guidelines to have in mind

RACI2025

Contains Nonbinding Recommendations

Computer Software Assurance for Production and Quality System Software

Guidance for Industry and Food and Drug Administration Staff

Document issued on September 24, 2025.

The draft of this document was issued on September 13, 2022.

For questions about this document regarding CDRH-regulated devices, contact the Compliance and Quality Staff at 301-796-5577 or by email at CaseforQuality@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010, or by email at ocod@fda.hhs.gov.



U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research



EN

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Public Health

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CONSULTATION | Open

Stakeholders' Consultation on EudraLex Volume 4 - Good Manufacturing Practice Guidelines: Chapter 4, Annex 11 and New Annex 22

Revision of Good Manufacturing Practice (GMP) Guidelines Chapter 4 (Documentation), Annex 11 (Computerised Systems) and New Annex 22 (Artificial Intelligence)

Page contents

Details
Target audience
Why we are consulting
Respond to the consultation
Reference documents

Details

Status	OPEN
Opening date	7 July 2025
Deadline	7 October 2025, 23:59 (CEST)
Department	Directorate-General for Health and Food Safety

Target audience

Public health stakeholders involved in GMP activities

The organisations representing stakeholders involved in GMP activities are encouraged to take part in the consultation and to receive all the comments of this consultation from their members, to compile and send the comments via the EU Survey tool.

Why we are consulting

In light of the rapid advancement of digital technologies and the implementation of AI systems in pharmaceutical manufacturing, the update of Good Manufacturing Practice (GMP) guidelines is essential to ensure that they continue to provide clear, practical and relevant guidance for manufacturers and national competent authorities.

The revision of GMP Annex 11 and Chapter 4, along with the introduction of a dedicated Annex 22 on Artificial Intelligence aim at supporting innovation in the manufacturing of medicines and ensuring regulatory harmonisation.

To maintain the global alignment of standards, achieving at the same time assurance for the highest quality, these 3 documents have been drafted by the EMA GMDP-Inspectors Working Group in cooperation with the PIC/S.

Revision of Chapter 4 - Documentation

The revised Chapter 4 incorporates changes which highlight the importance of documentation in GMP compliance and support the use of new technologies, hybrid solutions, and new services in the management of documentation. Risk-management principles are now central and integrated within the data governance system to ensure the accuracy, integrity, availability, and legibility of documents across all

AI/ML Validation

RACI2025

ARTIFACT	DATA	ALGORITHM	MODEL	MODEL VALIDITY	VALIDATION
URS/SRS	Data sources	Purpose Intended use	Input feed Output consumption	Expected range of confidence	PQ
FS	DOE Coverage Training/testing Contextualization	Generic/Ad-hoc Maths & Statistics Justification Inputs/outputs	Results Format Model Metadata Life cycle Audit	Accuracy Performance Efficiency Confusion Matrix	OQ
DS	Methods and scripts Clean-up and preprocessing	Fine tuning Hyperparameters	Storage Execution	Fine tuning Triangulated validity	IQ
Risk Assessment	Bias Clean-up criteria Processing Automation	Conditioning Variability Complexity Continuous Learning	Computing and storage capabilities Monitoring Overfitting/underfitting	Data divergence Data drift	Continuous monitoring

Source: [AI Empowering Process Analytical Technology and Continued Process Verification in Biotechnology](#)

AI Model Validation

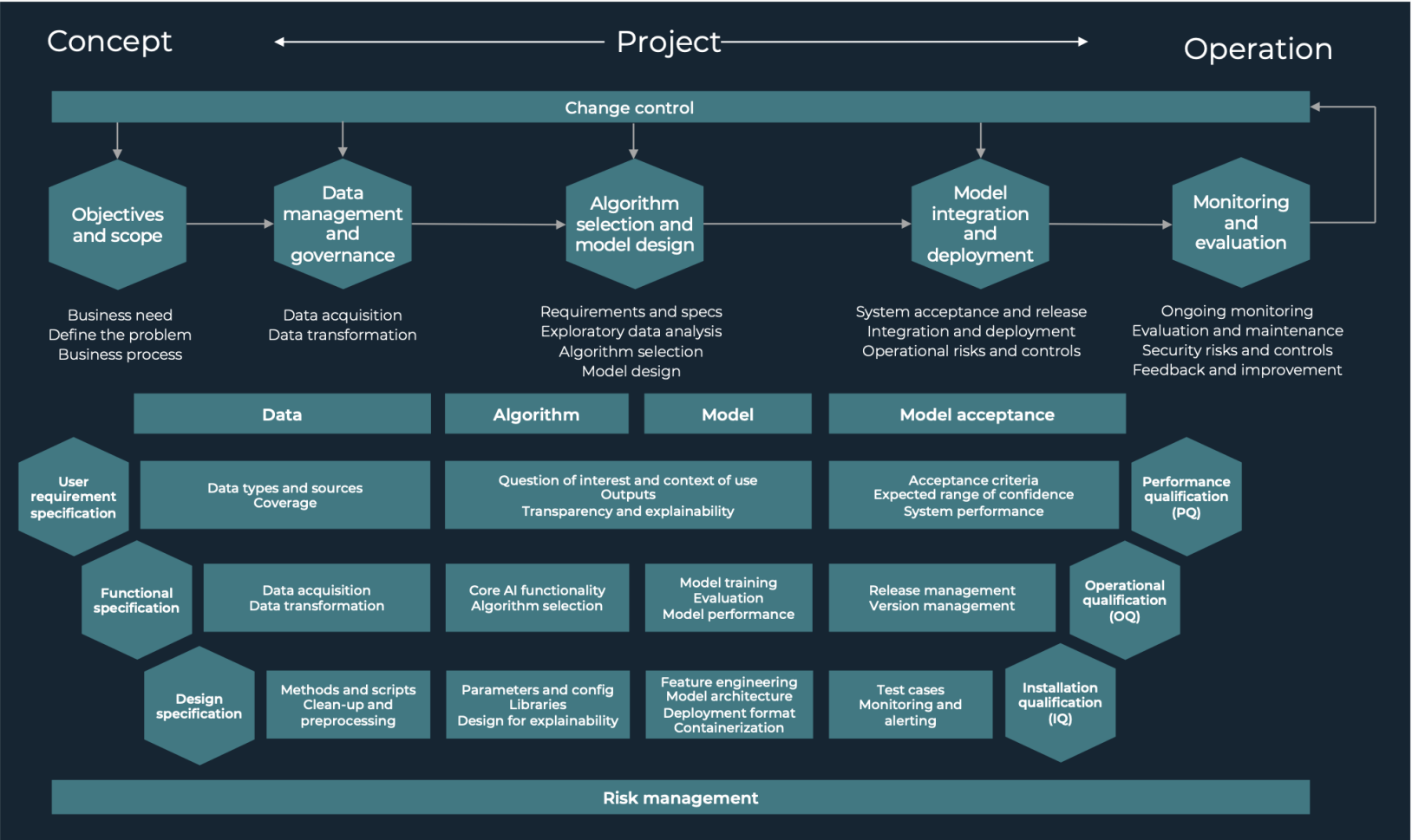
RACI2025



AI VALIDATION
Implementing AI systems in regulated pharma environments



CONNECT
 COLLABORATE
 ACCELERATE™



Science

WHO seeks innovative regulatory practices for greener pharmaceuticals

By **Nkechi Onyedika-Ugoeze, Abuja**

02 January 2025 | 2:22 am



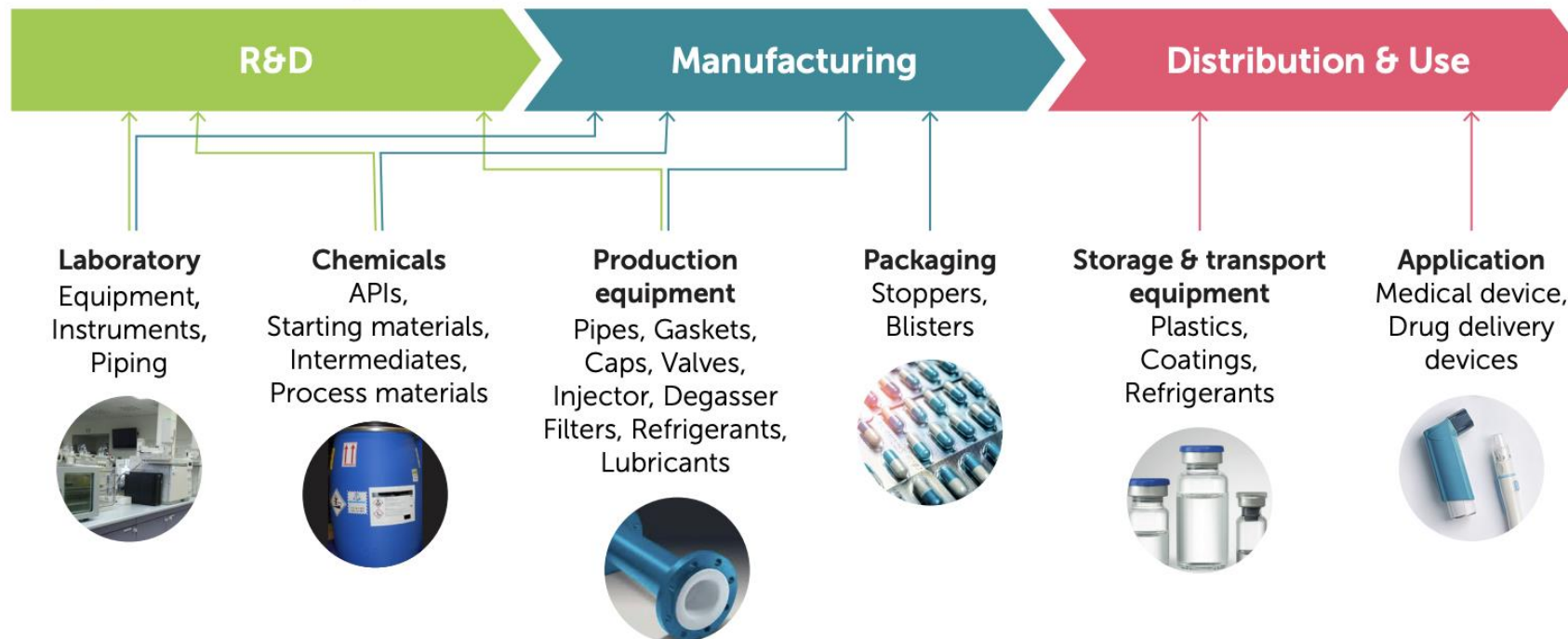
The World Health Organisation (WHO) has called for innovative regulatory practices to reduce the environmental footprint of medical products. The Department of Regulation and Prequalification in a document entitled “[Greener pharmaceuticals’ regulatory highway](#),” also expressed an urgent need to drive sustainability in the pharmaceutical sector, while maintaining high standards of safety and efficacy. WHO Assistant Director-General for Access to Medicines and Health Products, Dr Yukiko Nakatani, said addressing the environmental impact of healthcare products is no longer optional but imperative.

98%
of the Market Authorisations
of innovative medicines would
need to be amended

93%
of the EU's active substance
manufacturing relies
on fluoropolymers⁴

>70%
of critical medicines in European
Member States could be in short
supply

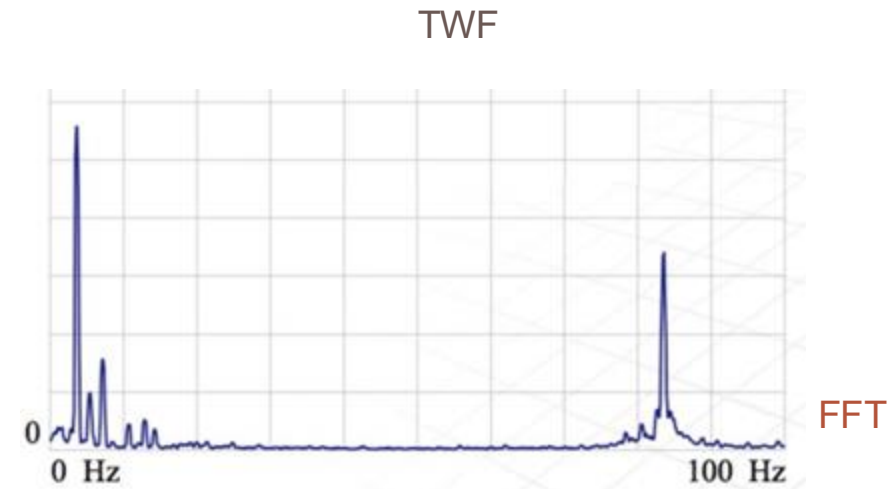
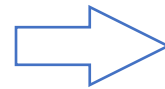
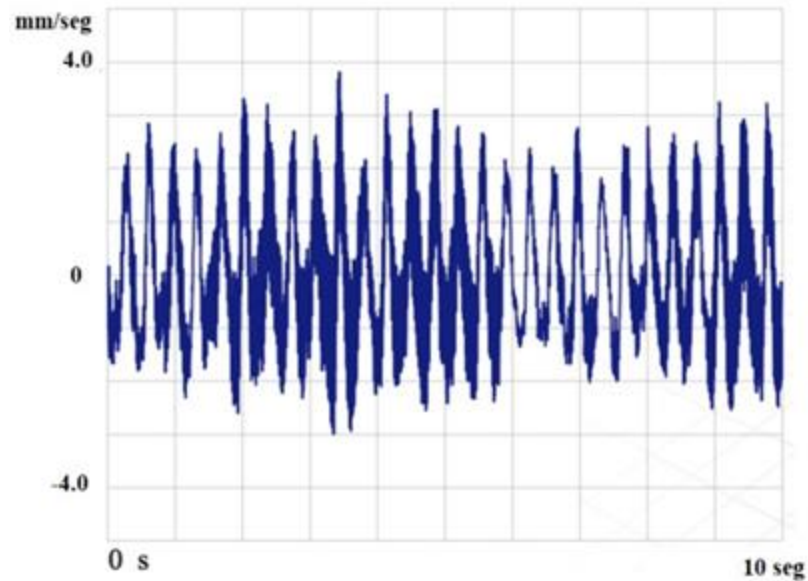
Examples of the widespread impact:



Overall Equipment Effectiveness (OEE)

RACI2025

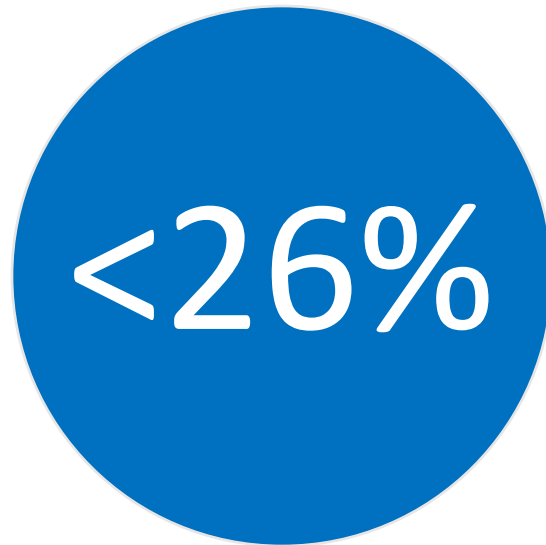
The information is in the noise/vibration level and the spectra of that noise



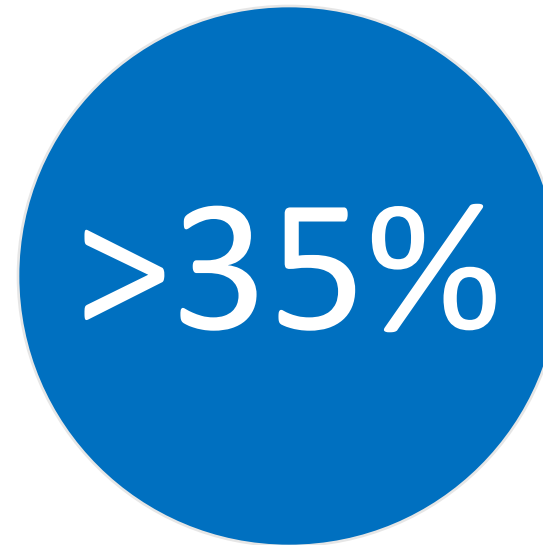
Overall Equipment Effectiveness (OEE)

RACI2025

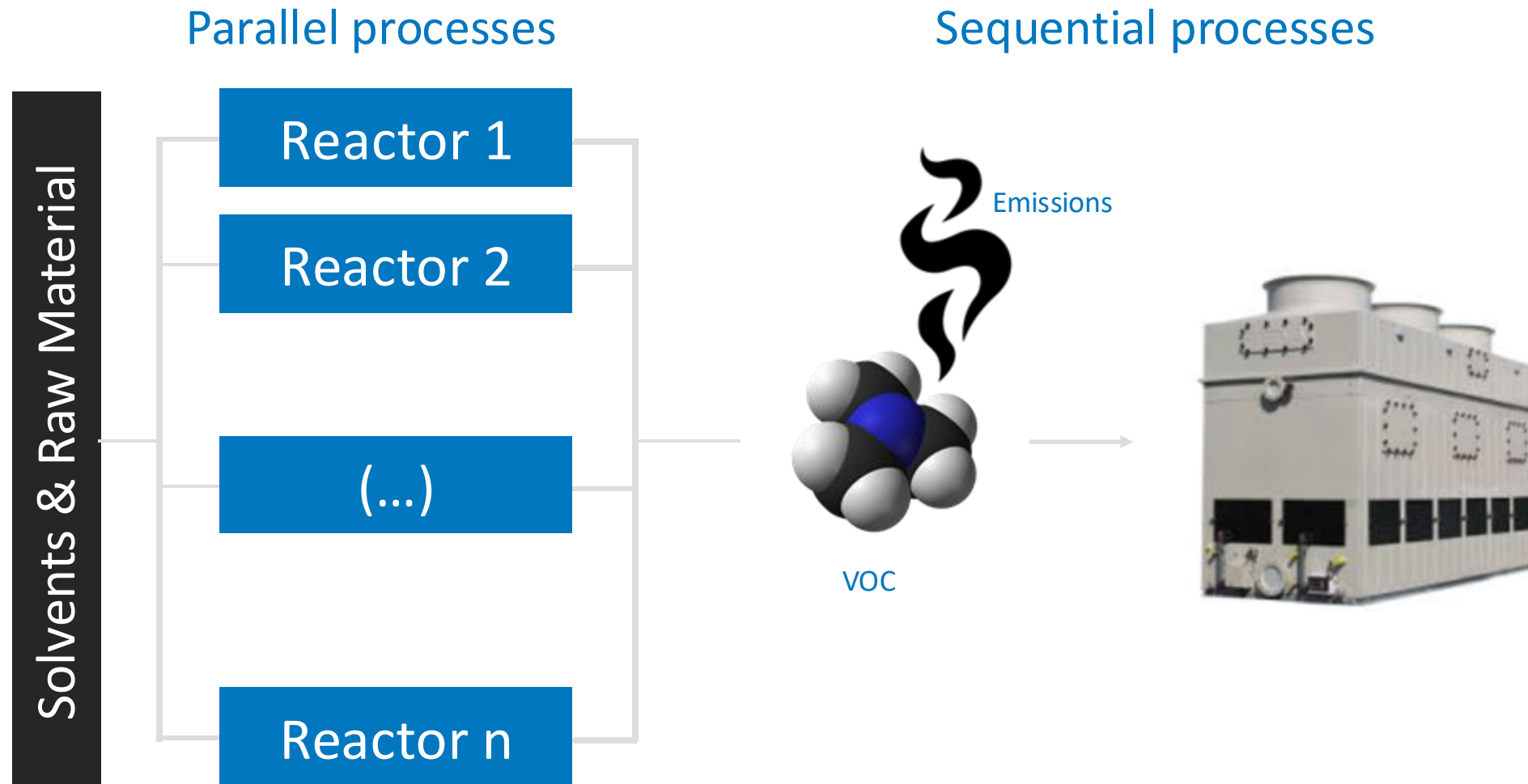
After a 6 months using IIoT, cloud and AI, the amount of 26% unexpected downtimes were reduced, the OEE increased a 35%

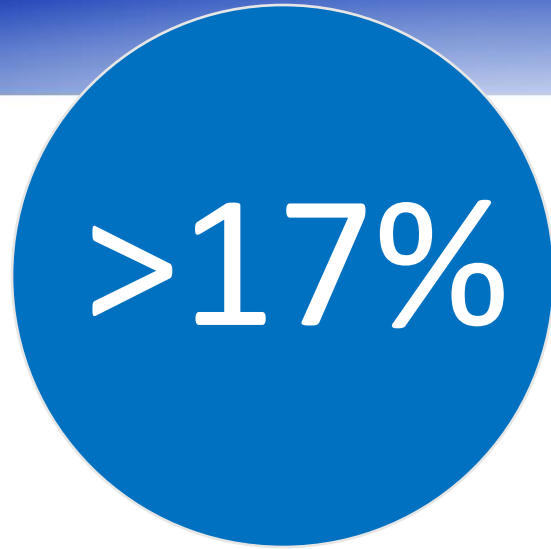


Downtimes



OEE > 35%





Energy savings






EL >20% x 1h

After a 2-month POC, 17% energy savings in the cooling processes, and no EL incidents (previously several per month)

Prescriptive Operator Guidance


RACI2025


Vessel 3 - Batch	Vessel 4 - Batch
16420081LOT1	16412709LOT1
Expected Finish: 06 Jun 2023 15:10:29	Expected Finish: 06 Jun 2023 13:53:21
Vessel 3 - Batch 15286454	Vessel 4 - Batch 15265227
Expected Finish: 19 Nov 2020 19:45:15	Expected Finish: 19 Nov 2020 13:20:40
Progress at 19 Nov 2020 12:31:23	Progress at 19 Nov 2020 12:31:23
	
Phases	
Current: SAMPLE_EXCIP_PH:1-1 Started at: 06 Jun 2023 08:12:22 Expected end: 06 Jun 2023 08:47:06	Current: TRANSFER_TPLATE:1 Started at: 05 Jun 2023 08:12:22 Expected end: 06 Jun 2023 08:47:06
Next Op. Interaction » ADD_FIBC:1-1 »  2	Next Op. Interaction: -
Starting at: 🕒 06 Jun 2023 08:47:09	Starting at: -



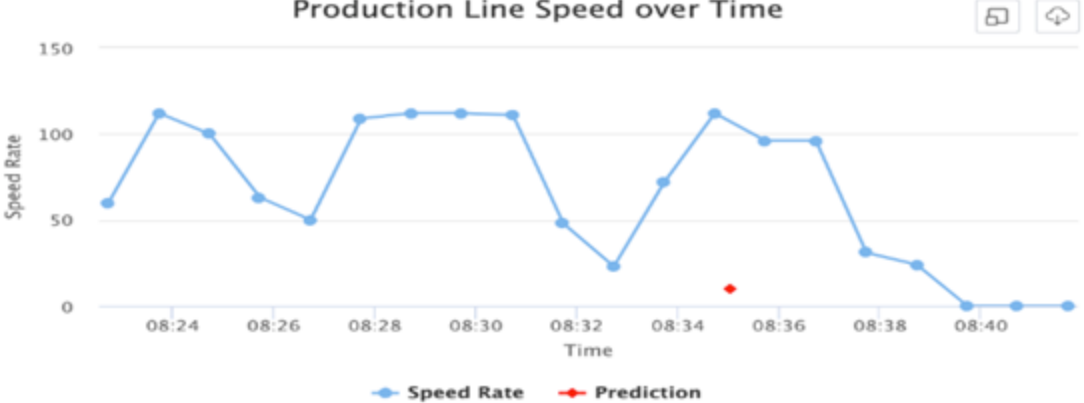

Creating alarms for human understanding

RACI2025

Stop duration	Room	Reaction time	Critical Zone	Ideal expected time	Theoretical expected time
5- mins	Capper Room	5+ mins		17-May-2023 17:39	17-May-2023 17:52

Stop alarm	
------------	--

Operator Feedback	
<input type="checkbox"/> Action taken	<input type="checkbox"/> No action taken

Production Line Speed over Time

Speed Line Slowing Down


Identifying relevant factors

Recognizing patterns

Recommending actions

Detecting anomalies

Predicting deviations

Establishing improvements

Executing repetitive analysis

Simulating processes

**Working closely with humans,
full commitment with patients!**

THREE COMMANDMENTS
Safety, Efficiency, Quality

ONE REQUIREMENT
**Keep the Human
Healthy**

A CURRENT NEED
**Speed, accuracy
and fast deployment**



Obrigado pelo seu tempo

toni.manzano@aizon.ai