



AI in Manufacturing of Pharmaceutical Products: Challenges and Opportunities

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Major Research Areas



Analytical Science



- Chromatography (e.g., HPLC and UPLC core facility)
- **Mass spectrometry (e.g., high throughput RapidFire)**
- Nuclear magnetic resonance (NMR) spectroscopy
- **Advanced separation (e.g., field flow fractionation)**
- Product performance (e.g., dissolution, in vitro release test, IVRT)
- Bioanalytics
- Shelf-life Extension Program (SLEP)

Formulation Science



- Oral solids (e.g., tablets, capsules)
- Topicals and transdermal
- Ophthalmic
- Injectables (e.g., liposomes, lipid-nanoparticles, suspensions, emulsions, long-acting)
- Implantable (e.g., intravaginal, intrauterine, intramuscular)
- Biopharmaceutics (e.g., IVIVC, BCS, bioequivalence, bioavailability)
- **Nanotechnology**
- All other complex formulations
- Excipients functionality (e.g., polymeric materials)
- Quality-by-Design (QbD)

Adv. Manufacturing



- **Continuous manufacturing (drug substances, solid oral dosage forms, complex formulations)**
- 3D printing
- Process analytical technology (PAT)
- Biomanufacturing (e.g., upstream/downstream processing, lyophilization)

Modeling & Simulation



- Digital twins
- In vitro in vivo correlation (IVIVC)
- Modeling, e.g., CFD, MD, DEM, RTD
- System/Process design (e.g., LabVIEW)
- **Data science**, e.g., AI/ML, chemometrics

Challenges

- Historical Data
- Operational Data
- Process Data
- Maintenance Data

Causes



Infinite Data Generation

Challenges



- Lack of connectivity
- Lack of context
- Lack of transparency
- Need for manual data preparation
- Fragmented and inconsistent data
- Lack of knowledge
- Limited automation

Reasons



- Significant time spent on preparing vs analyzing data
- Limited data are being used for reporting, analysis, and decision making
- Very few data are being analyzed and acted upon real-time

Solutions

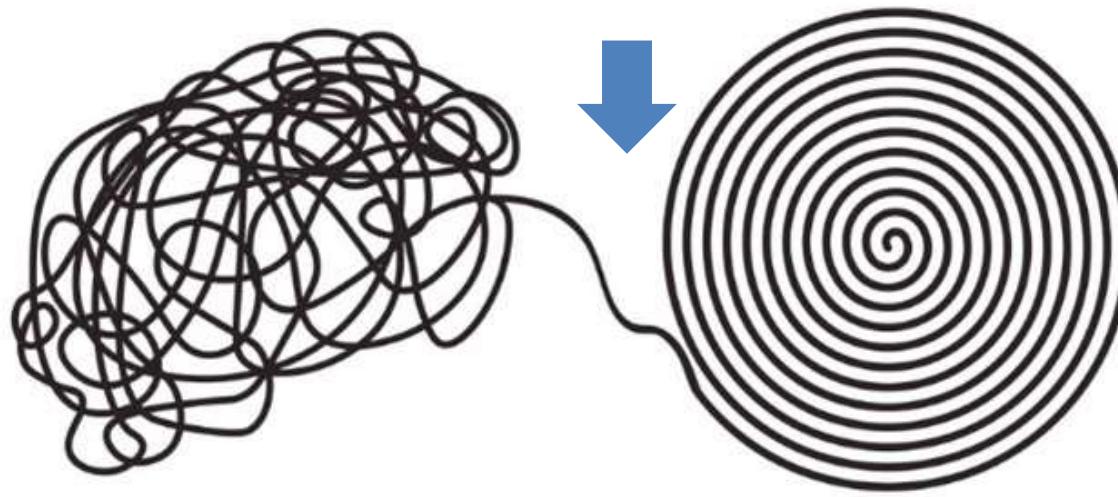


Digital Transformation | Data Integration | Data Contextualization

Opportunities



AI/ML Application



DATA

INFORMATION

Capture, Process, Organize Information; Perform Analysis; Uncover Actionable Insights

Use Case I: Study formulation design using ML applications



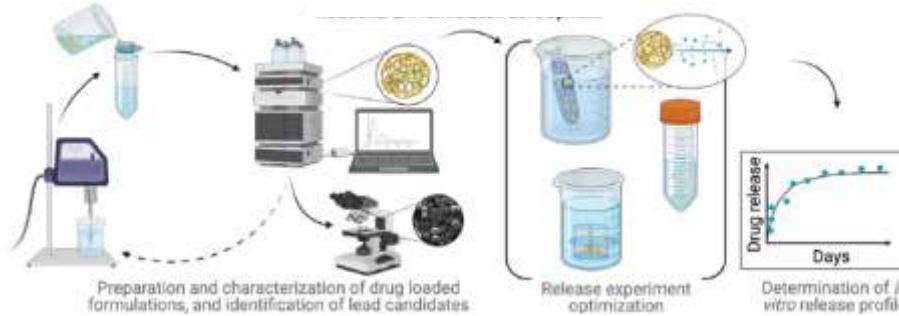
Careful design of formulations:

- Enhance efficacy of a new drug molecule
- Reduce adverse effect
- Improve bioavailability
- Reduce off-target delivery

Challenges in Formulation Design



Each drug has its own unique physicochemical properties



For a given material, there are wide range of variables that must be optimized during formulation preparation



Trial-and-error in the experiment design

Extensive resources



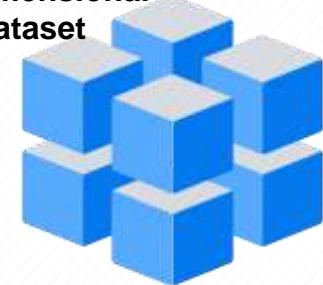
Time



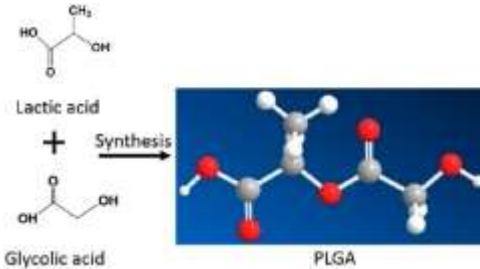
Cost



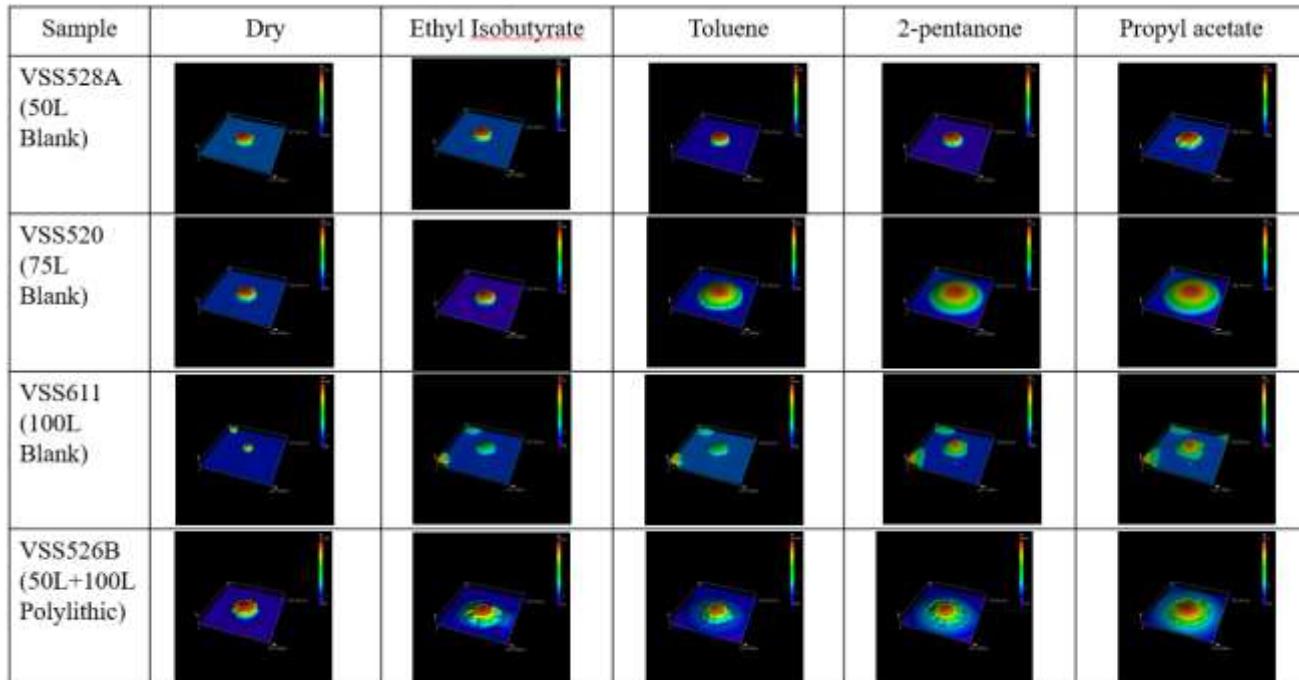
Multidimensional large dataset



PLGA-based Formulation Dataset

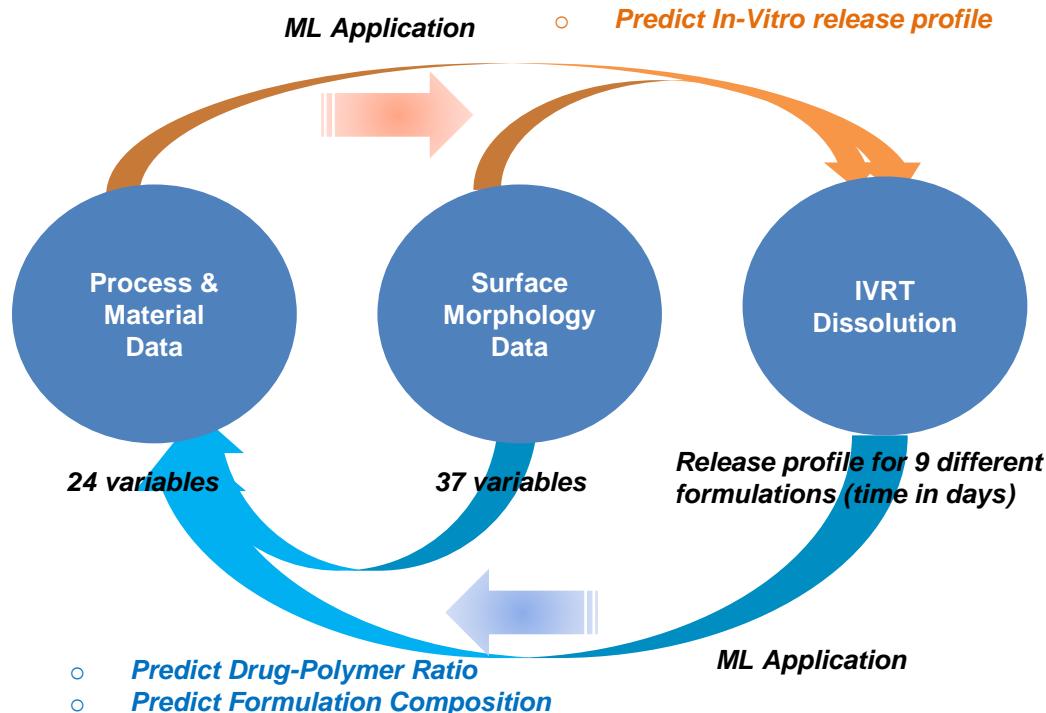


- Biodegradable poly(lactide-co-glycolide) (PLGA) microparticles have been used as long-acting injectable (LAI) drug delivery systems from past three decades.
- Used for **prolonged therapeutic effect** and become the ideal formulation strategies for treatment of **chronic disease**.



** The dataset for this study was derived from a previous FDA-funded research project at Akina, Inc. (BAA#75F40119C10096).

Analysis



Significant Parameters Selection

Predict Drug -Polymer ratio

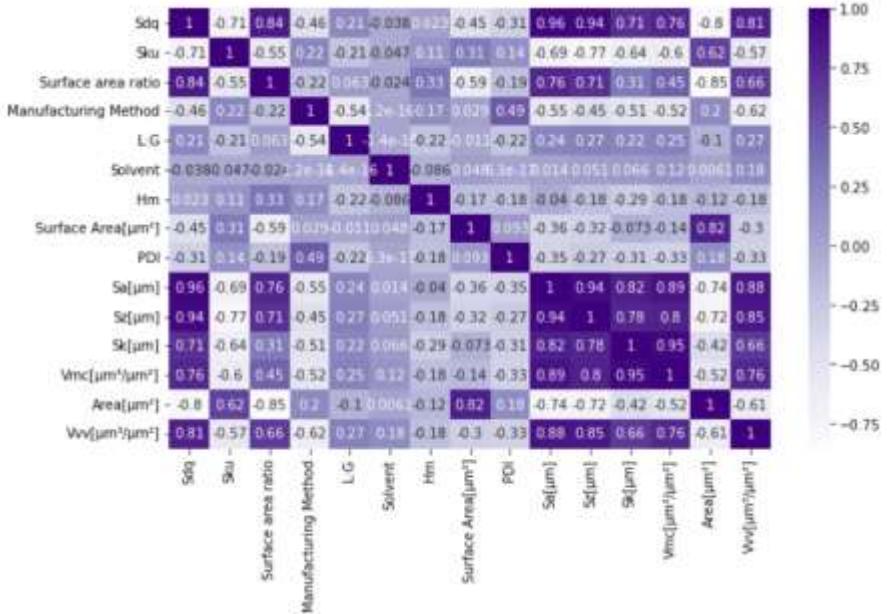
Predict Formulation Composition

Predict In-vitro release behavior

Overall Predictive Performance



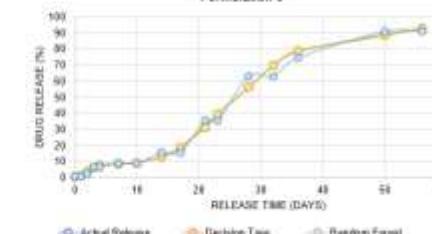
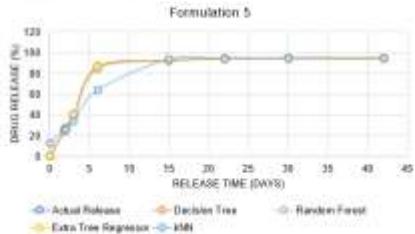
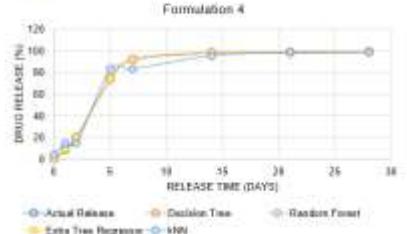
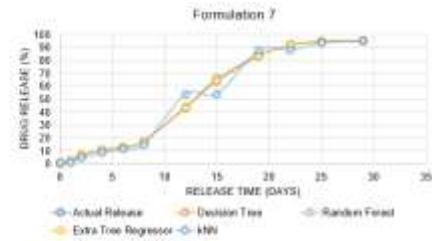
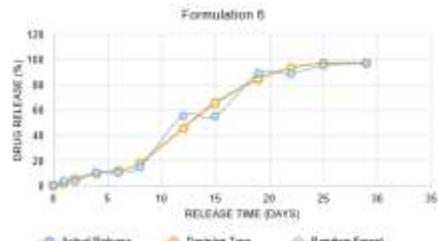
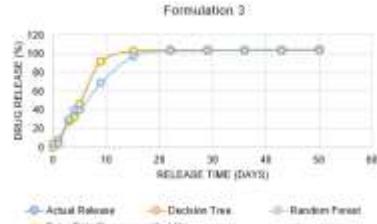
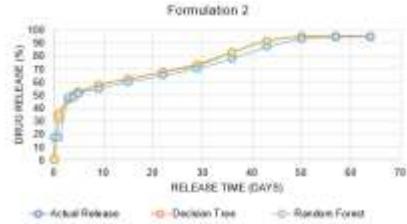
Correlation Matrix



Prediction of Formulation Composition				
Machine Learning Techniques	MSE	MAE	Accuracy (%)	
Linear Regression	0.001	0.02	99.5002	
Decision Tree	0	0	100	
Random Forest	0.3439	0.4	90	
Extra Trees Regressor	0.0042	0.0289	99.2778	

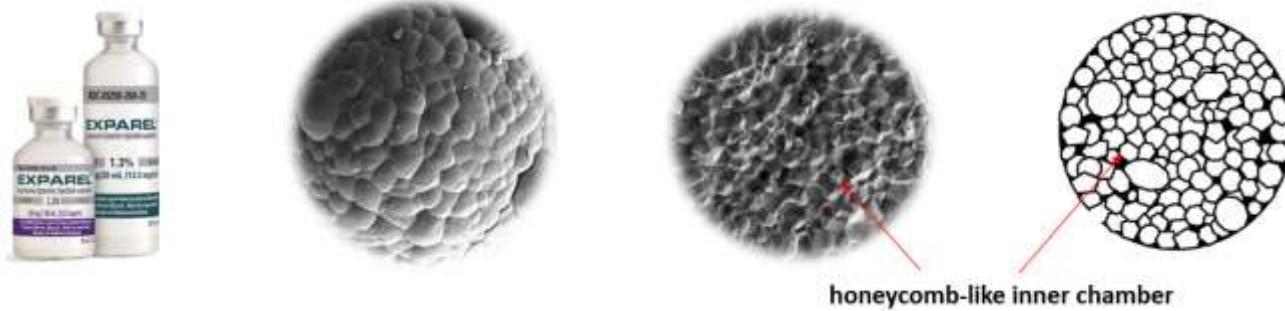
Prediction of Drug – Polymer Ratio				
Machine Learning Technique(s)	MSE	MAE	Accuracy (%)	
Logistic Regression	0	0	100	
Decision Tree	0	0	100	
Random Forest Regressor	0	0	100	
Artificial Neural Network (ANN)	0.0021	0.0378	78	

In-Vitro Release Prediction



- This AI method may serve as a tool in the future to help comparing the proposed generic products to reference listed drugs (RLD) by analyzing feature similarity across different formulations.
- Such a tool may also help addressing some of the unique challenges in determining the bioequivalence of long acting injectable generic products.

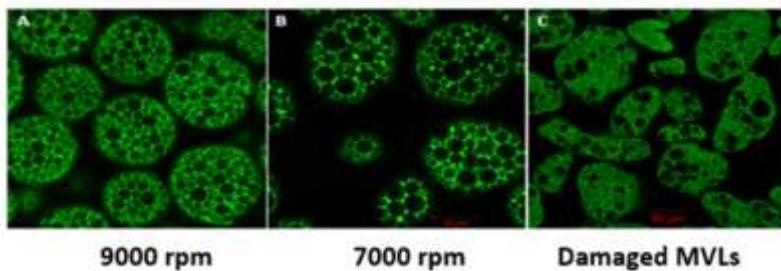
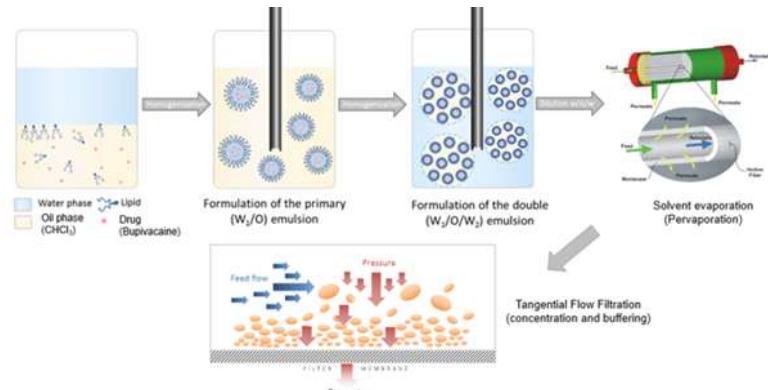
Use Case II: Advanced Imaging Analysis to Improve understanding of Multivesicular Liposomes



- Multivesicular liposome (MVL) is a lipid based drug delivery system for sustained release of the drugs with short half lives.
- Multivesicular Lipid Liposomes (MVLs) are complex and oftentimes sensitive to the release environment.
- Design and development of appropriate in vitro release test (IVRT) method is challenging for MVLs.

AI-assisted image analysis

The study aims to **develop AI assisted image analysis** method to provide **quantitative assessment** of the MVL morphology changes due to process parameter changes.



Segmentation & Templating

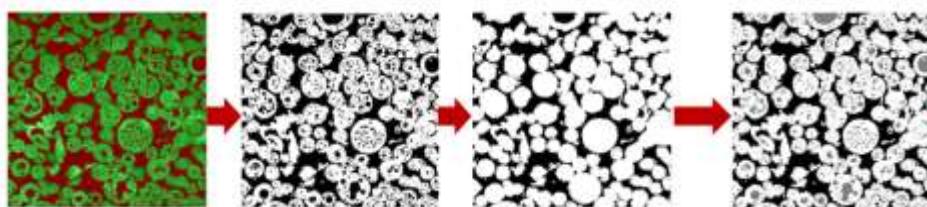
- Identify Particles, Pores, Background
- Create Template for different segmentation

Quantitation

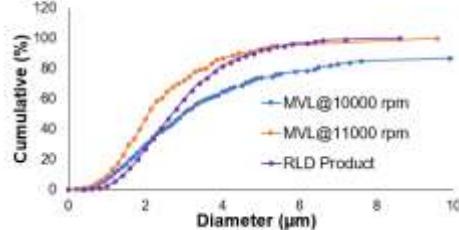
- Count and Measure

Output

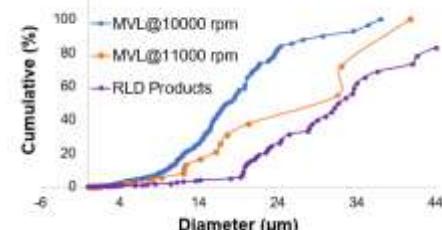
- External & Internal Particle Sizes
- Spatial Distribution



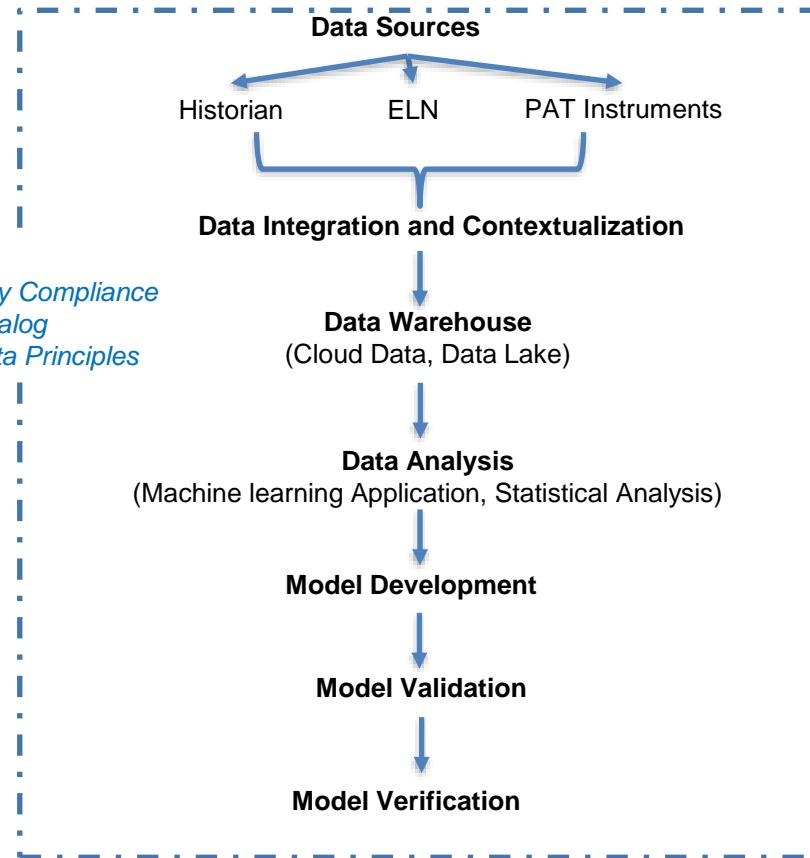
Internal Particle Size Distribution



External Particle Size Distribution



Data Architecture for Advanced Manufacturing



Required:

- *Regulatory Compliance*
- **Data Catalog*
- **FAIR Data Principles*

**FAIR (findability, accessibility, interoperability, reusability)*

**Data Catalog: detailed inventory of all data assets in an organization*

Closing Thought



- In advanced manufacturing, **data silos occur across different stages** of production process, including design, production, quality control, and supply chain management.
- The lack of **seamless data exchange and collaboration** among these domains can lead to inefficiencies, redundancies, and missed opportunities.
- To fully leverage the potential of **digital transformation** in advanced manufacturing, breaking down data silos is essential.
- The design process and its **outcome need to be transparent** for equipment manufacturer, pharma companies and regulatory agencies to achieve trust in every process step.

Acknowledgement

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Thank You



Questions?

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