Machine Learning for Sequential Process Optimization

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Pfizer

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Groton, CT

Pharmaceutical Sciences, Small Molecule
Drug Product Manufacturing

conneqt

Pfizer

Who We Are

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Our Business

$58.5B
REVENUE
in 2023

36
MANUFACTURING
sites worldwide

~87,000
COLLEAGUES
around the world

>181
COUNTRIES
in which Pfizer sells products

10
PRODUCTS
with sales greater than **$1B** in 2023

112
PRODUCTS
in Clinical Research and Development

Updated January 30, 2024

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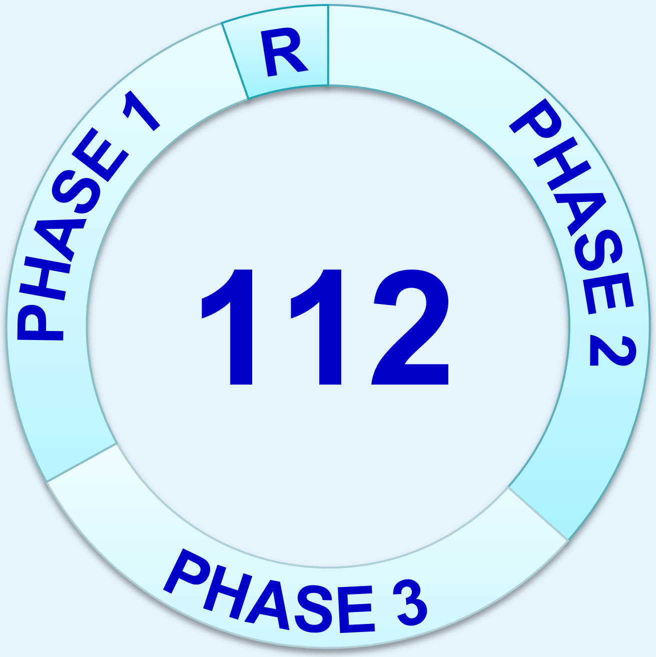
Updated January 30, 2024

Our Pipeline



DISCOVERY PROJECTS

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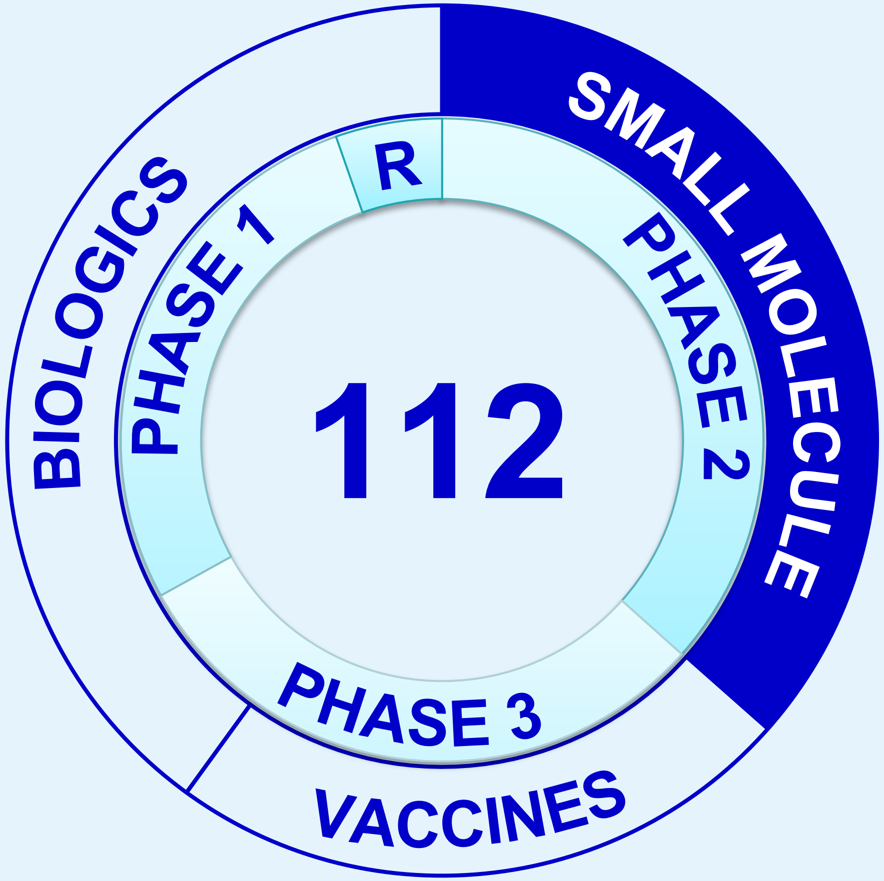
Updated January 30, 2024

Our Pipeline



DISCOVERY PROJECTS

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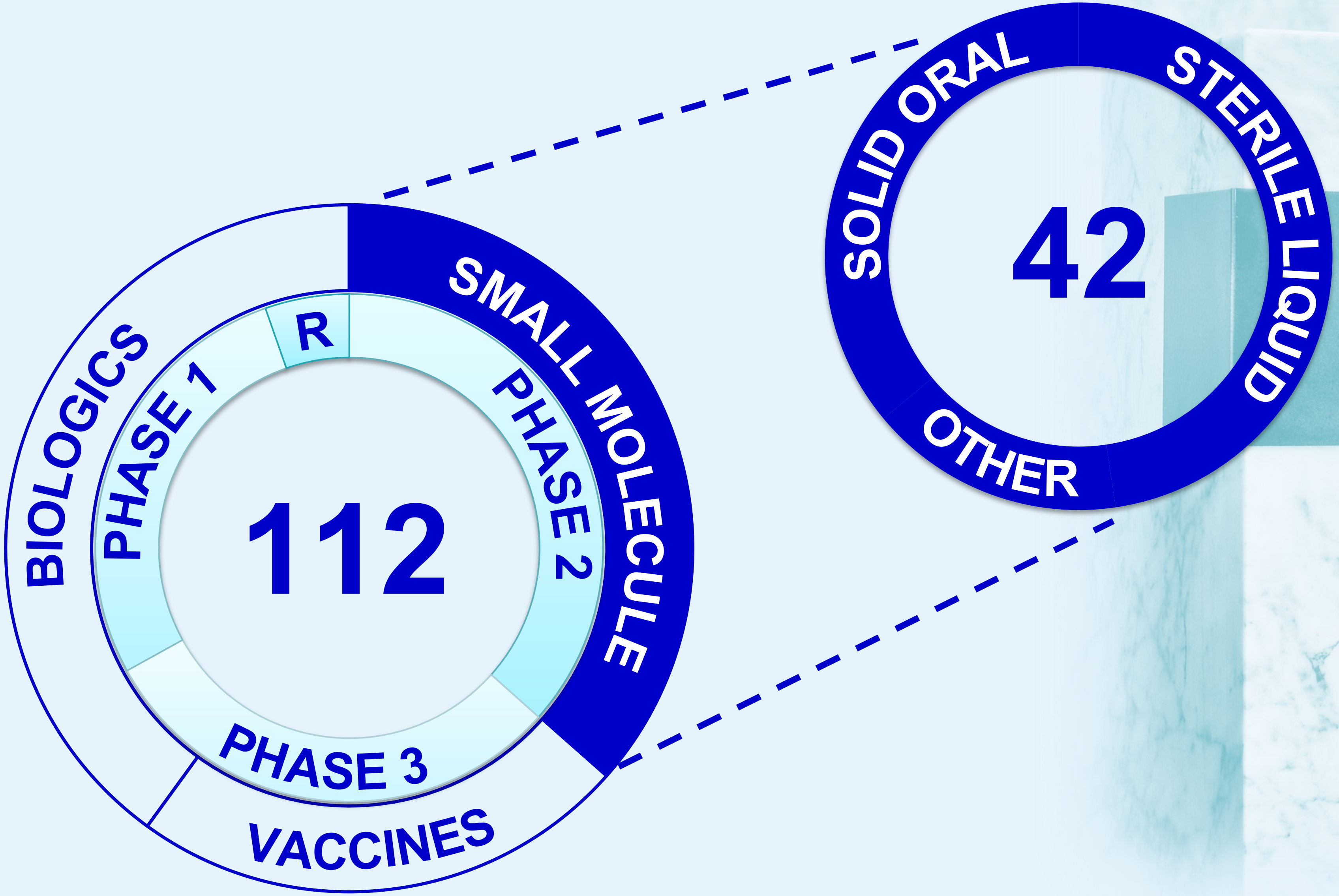

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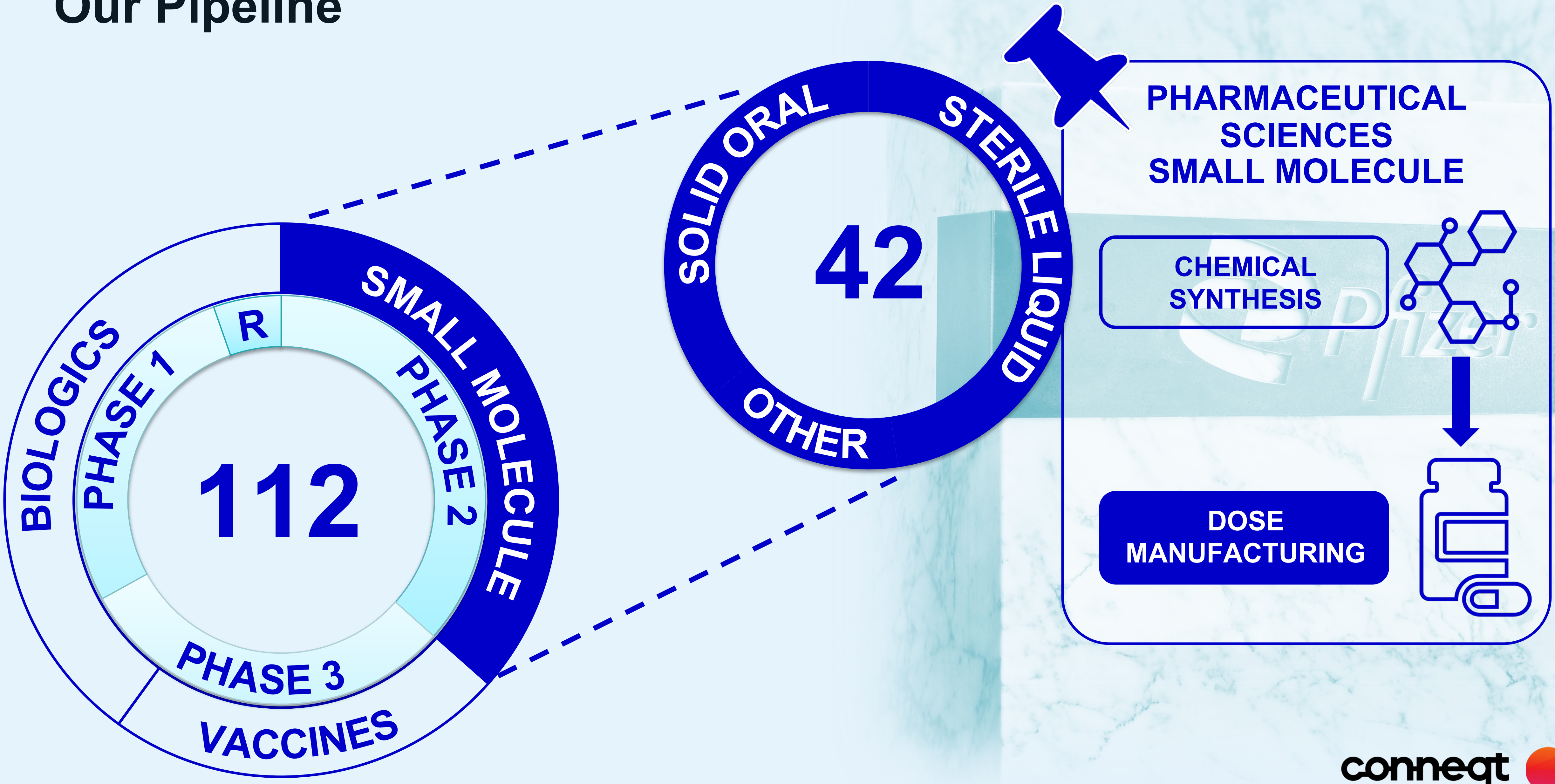

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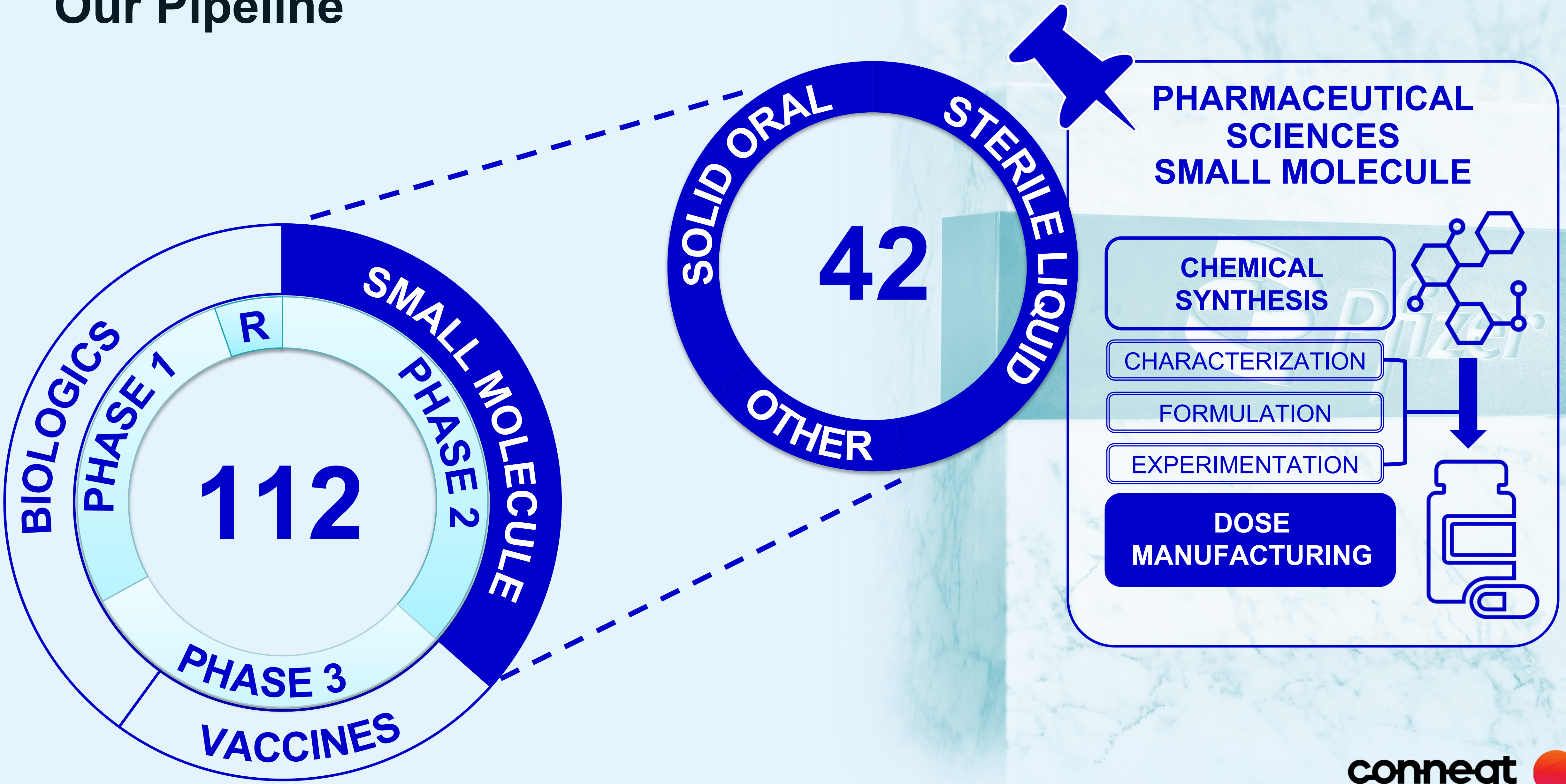

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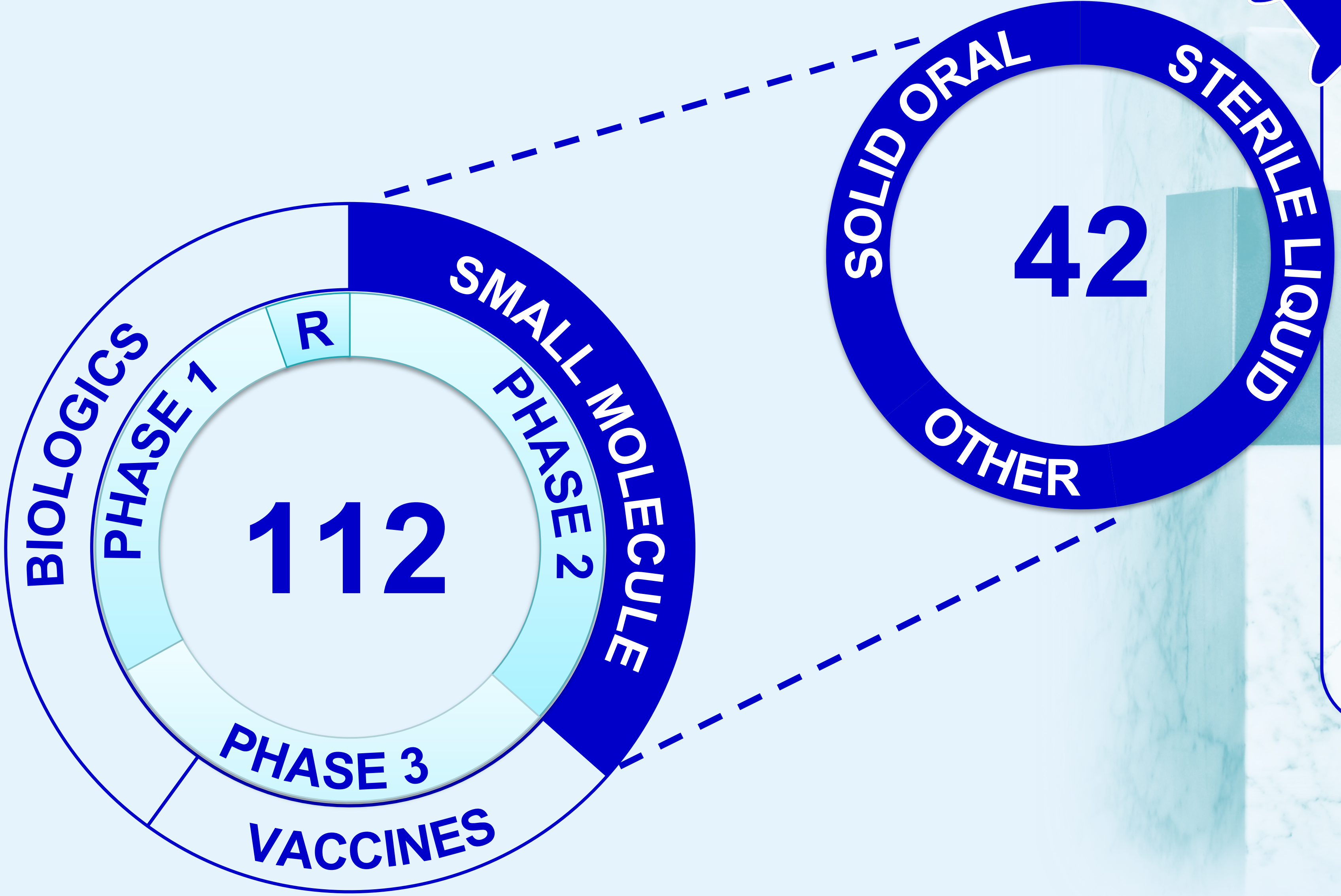
Our Pipeline



SMALL MOLECULE SOLID ORAL DOSAGE

- Capsules
- Multiparticulates
- Swellable Core Tablets
- Material-Sparing Tablets
- Functional Coating

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Our Organization

FIH	Phase 1	Phase 2a/b	Phase 3	Registration

WHEN WE MANUFACTURE

Our Organization

FIH | Phase 1 | Phase 2a/b | Phase 3 | Registration

PROJECT INTAKE

- Frequent First-Time Manufactures
- Variable Access to Material Information

SCALE-UP, COMMERCIAL PREP

WHEN WE MANUFACTURE

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Our Organization

FIH | Phase 1 | Phase 2a/b | Phase 3 | Registration

PROJECT INTAKE

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SCALE-UP, COMMERCIAL PREP

WHEN WE MANUFACTURE

CHALLENGES:

- **One Size Fit All**
- **Limited Product Experience**
- **High Product Turnover**

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What We Manufacture

What We Manufacture

PHARMACEUTICAL SCIENCES SMALL MOLECULE

- Capsules
- Multiparticulates
- Swellable Core Tablets
- Material-Sparing Tablets
- Functional Coating

What We Manufacture

PHARMACEUTICAL SCIENCES SMALL MOLECULE

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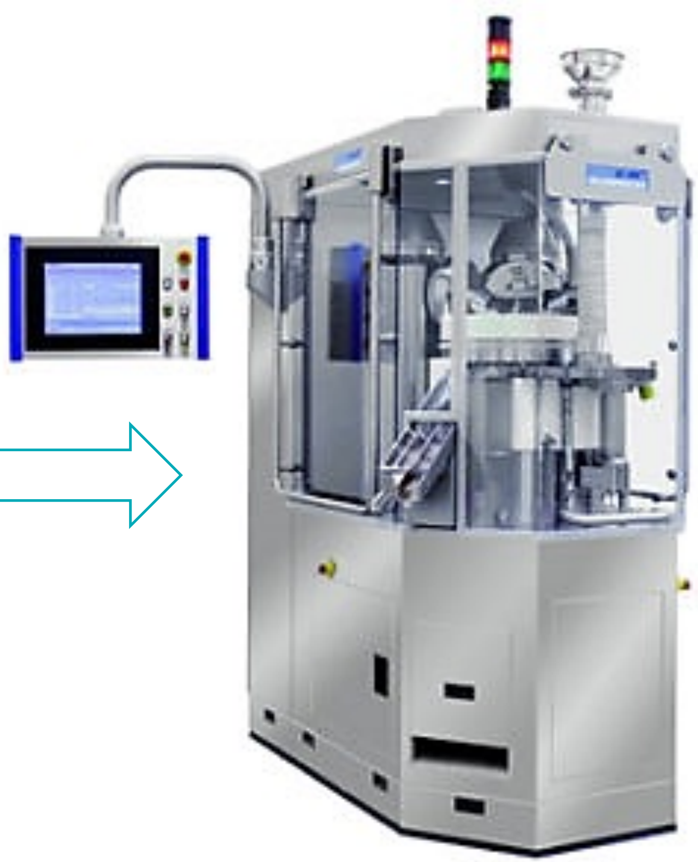
Material-Sparing Tablets

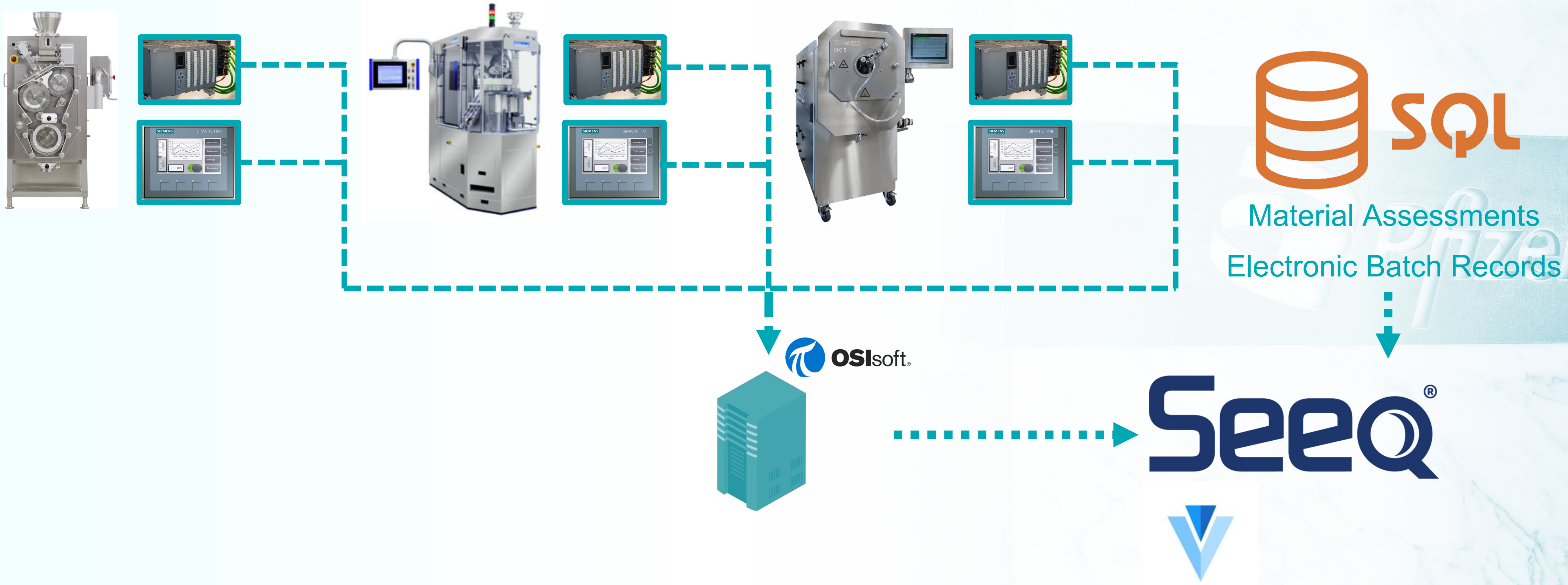
Compaction



Compression

Coating

Material-Sparing Tablets



Material-Sparing Tablets

Compaction

Losses:

Time: 30-min avg. Startup

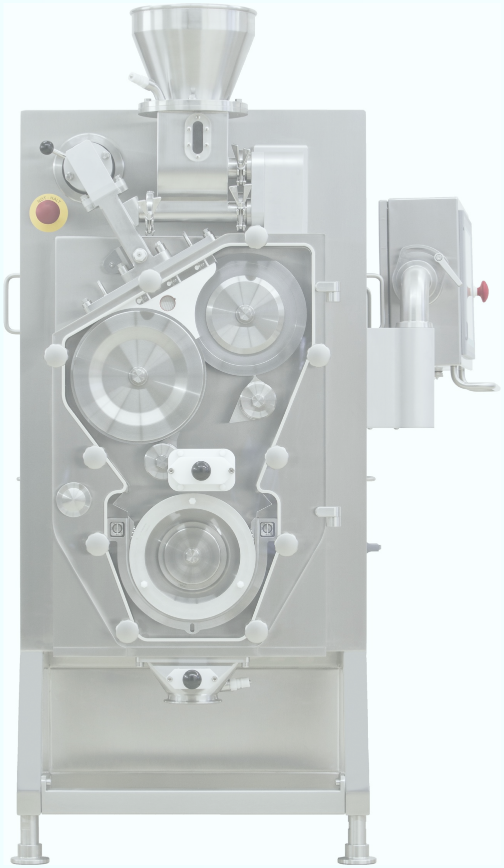
Material: N/A

Targeted Quality Attributes:

Ribbon Solid Fraction $= \frac{\rho_{ribbon}}{\rho_{true}}$

Necessary to reach target solid fraction prior to entering production.

Material-Sparing Tablets



Compaction

Losses:

Time: 30-min avg. Startup

Material: N/A

Targeted Quality Attributes:

Ribbon Solid Fraction

$$= \frac{\rho_{\text{ribbon}}}{\rho_{\text{true}}}$$

Compression

Losses:

Time: 30-min avg. Startup

Material: Startup Tablets, Rejects

Targeted Quality Attributes:

Tablet Weight

Tablet Thickness

Tablet Hardness

Exceeding product limits can result in potential loss of product

Our Constraints

Our Constraints

Resource Constraints

- Set number of machines available for operation
- Set number of trained operators

Material Constraints

- Limited, expensive active pharmaceutical ingredient (API)
- Set quantity of dispensed material

Time Constraints

- Firm delivery dates for clinical supply
- Clinical projects in queue

Our Needs

A digital, predictive tool

Our Needs

A digital, predictive tool…that

- ❑ **minimizes material waste**
- ❑ **shortens startup time**
- ❑ **builds process understanding over time**

Our Solution

Model Roadmap

Inputs

- True Density
- Drug Load
- Roll Design

API Particle Size

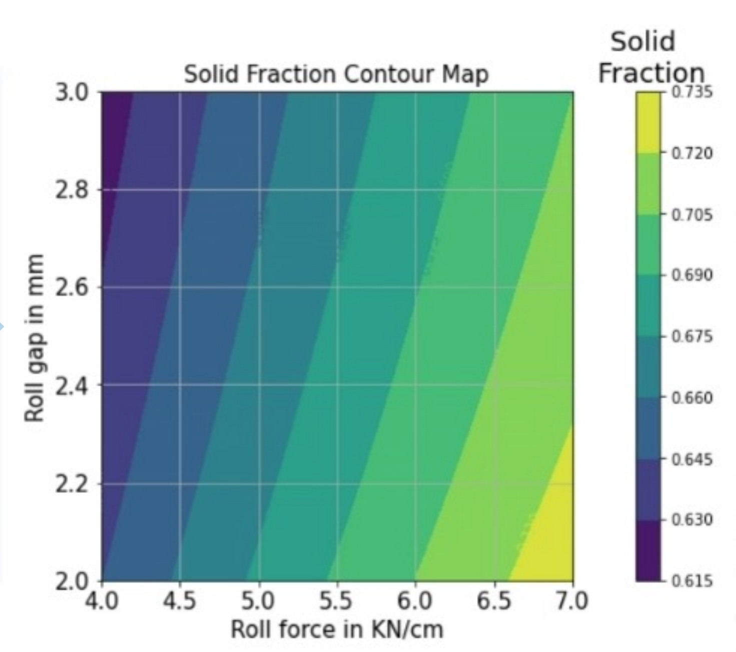
- SF Measurement Method (TP or PT)
- MCC Bulk Density

Model

Seeq DATA LAB

Outputs

Contour Map



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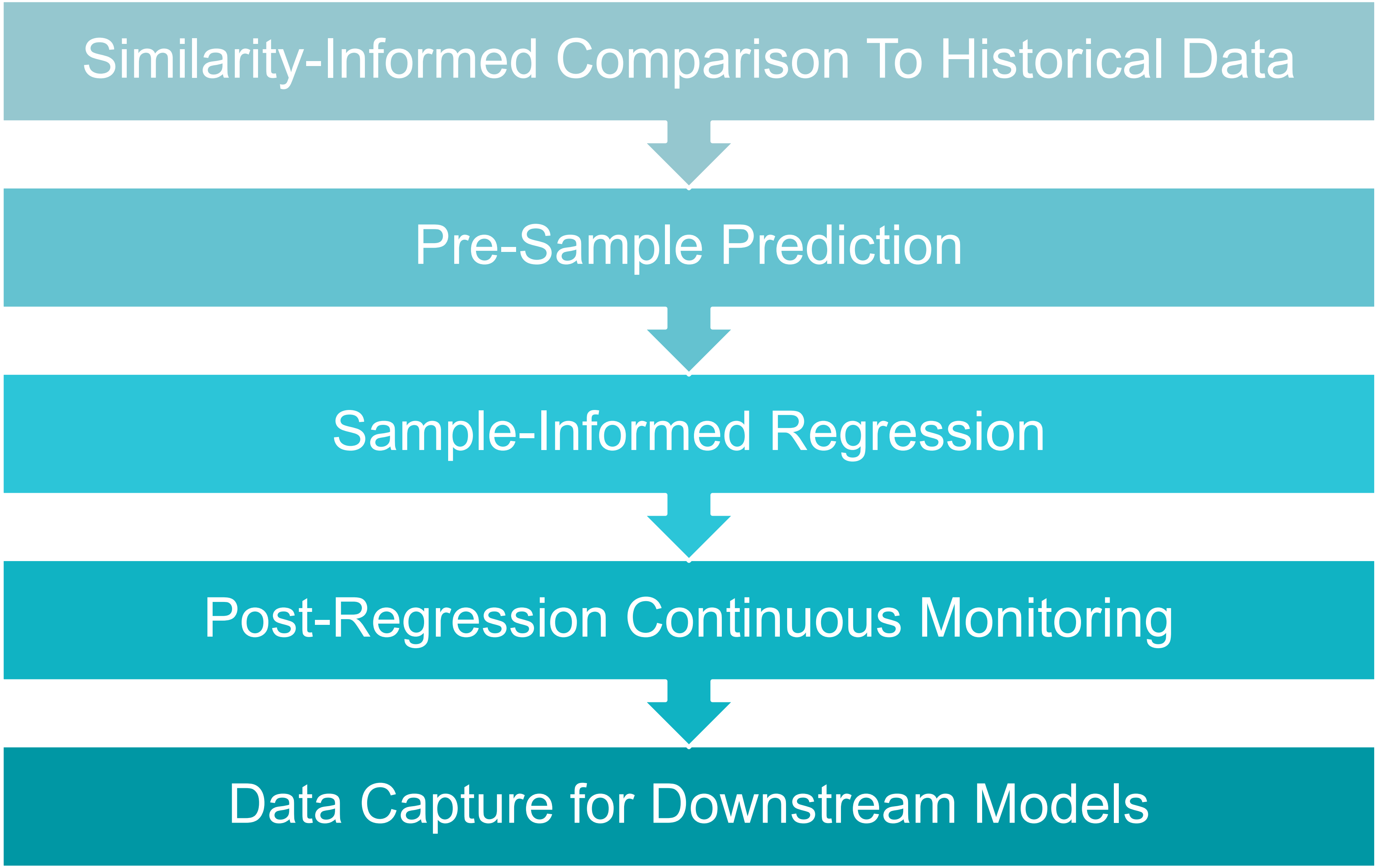
Model Design



Model Design

Techniques Used

Similarity-Informed Comparison To Historical Data — Unsupervised Learning (PCA Prioritization)

Pre-Sample Prediction — Supervised Learning (Random Forest)

Sample-Informed Regression — Online Learning (Next State Prediction)

Post-Regression Continuous Monitoring — Post-Hoc Model Fitting (Feed Forward)

Data Capture for Downstream Models

Model Design

Similarity-Informed Comparison To Historical Data

Pre-Sample Prediction

Sample-Informed Regression

Post-Regression Continuous Monitoring

Data Capture for Downstream Models

DATA LAB

Similarity-Informed Comparison To Historical Data

Steps

1) A new product is entered into the model.

Similarity-Informed Comparison To Historical Data

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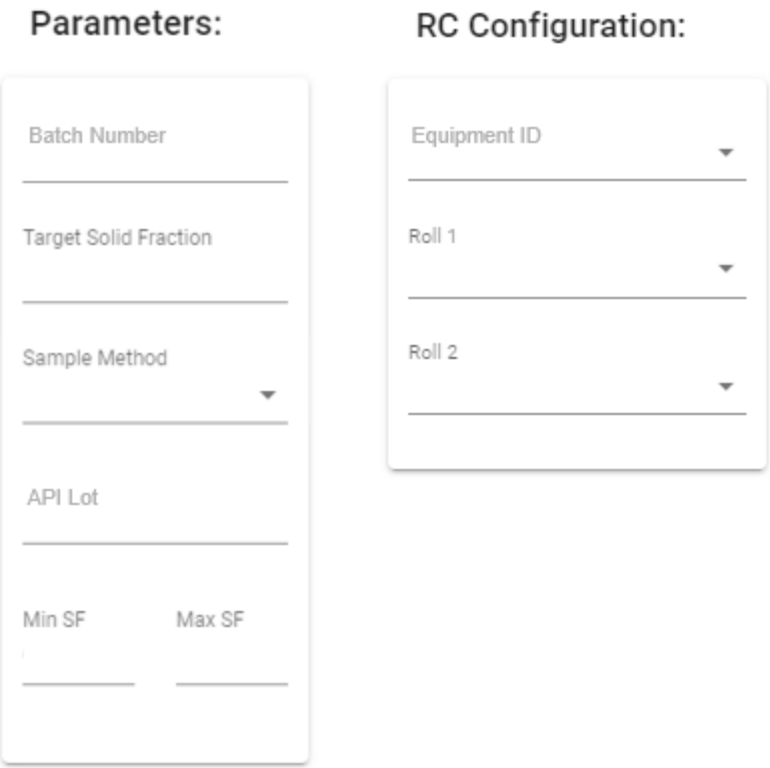

Similarity-Informed Comparison To Historical Data

Steps

1) A new product is entered into the model.

2) Similarity scores are then assigned to each previously recorded batch over multiple parameters:

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		$\{x_1, x_2, \dots, x_n\}$ $\{a_{i_1}, a_{i_2}, \dots, a_{i_n}\}$ for i blend attributes			
API Particle Size Shared area under size distribution regressions via BD[1]	Roll Design Scored as 100%, 50% similar, or 0% by # overlapping roll type	Blend Composition Currently limited to product class i.e., MST1.0, 2.0 etc., drug load, and true density	Compactor Used Boolean score evaluating (Ref Batch == Running Batch)	True Density Normalized to % Product Density	Recency Batches prioritized by recency to account for wear

Similarity-Informed Comparison To Historical Data

API Particle Size	Roll Design	Blend Composition	Compactor Used	True Density	Recency
		$\{x_1, x_2, \dots, x_n\}$ $\{a_{i_1}, a_{i_2}, \dots, a_{i_n}\}$ for i blend attributes			
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			OSIsoft		OSIsoft

Similarity-Informed Comparison To Historical Data

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Similarity-Informed Comparison To Historical Data

Available Similarity Index Contributors
Roll Design
Particle Size Distribution
Formulation Type (MST x.0)
Drug Load
True Density
Compactor Used
Recency

Only D10, D90 available

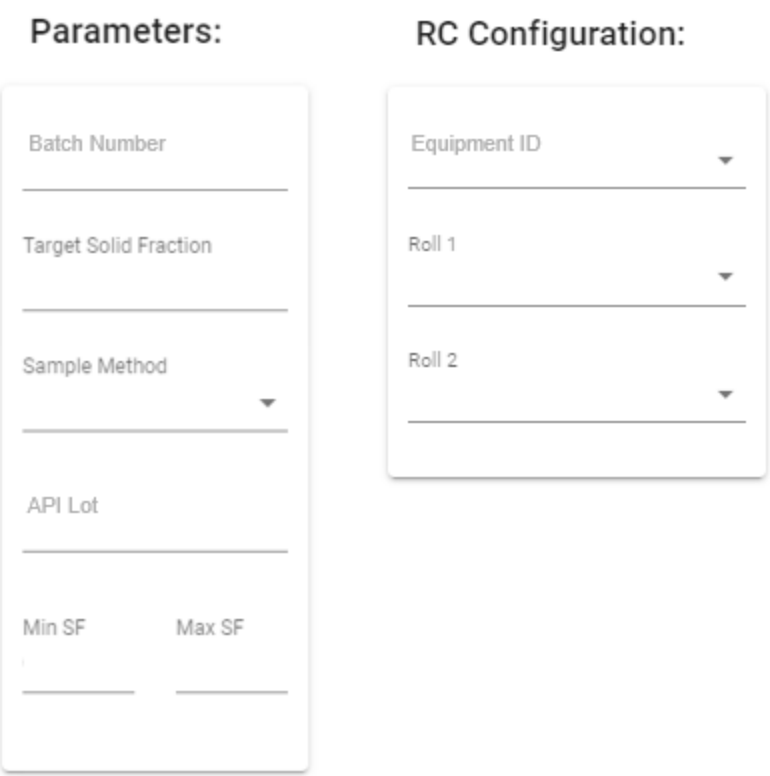
Compactor not yet allocated

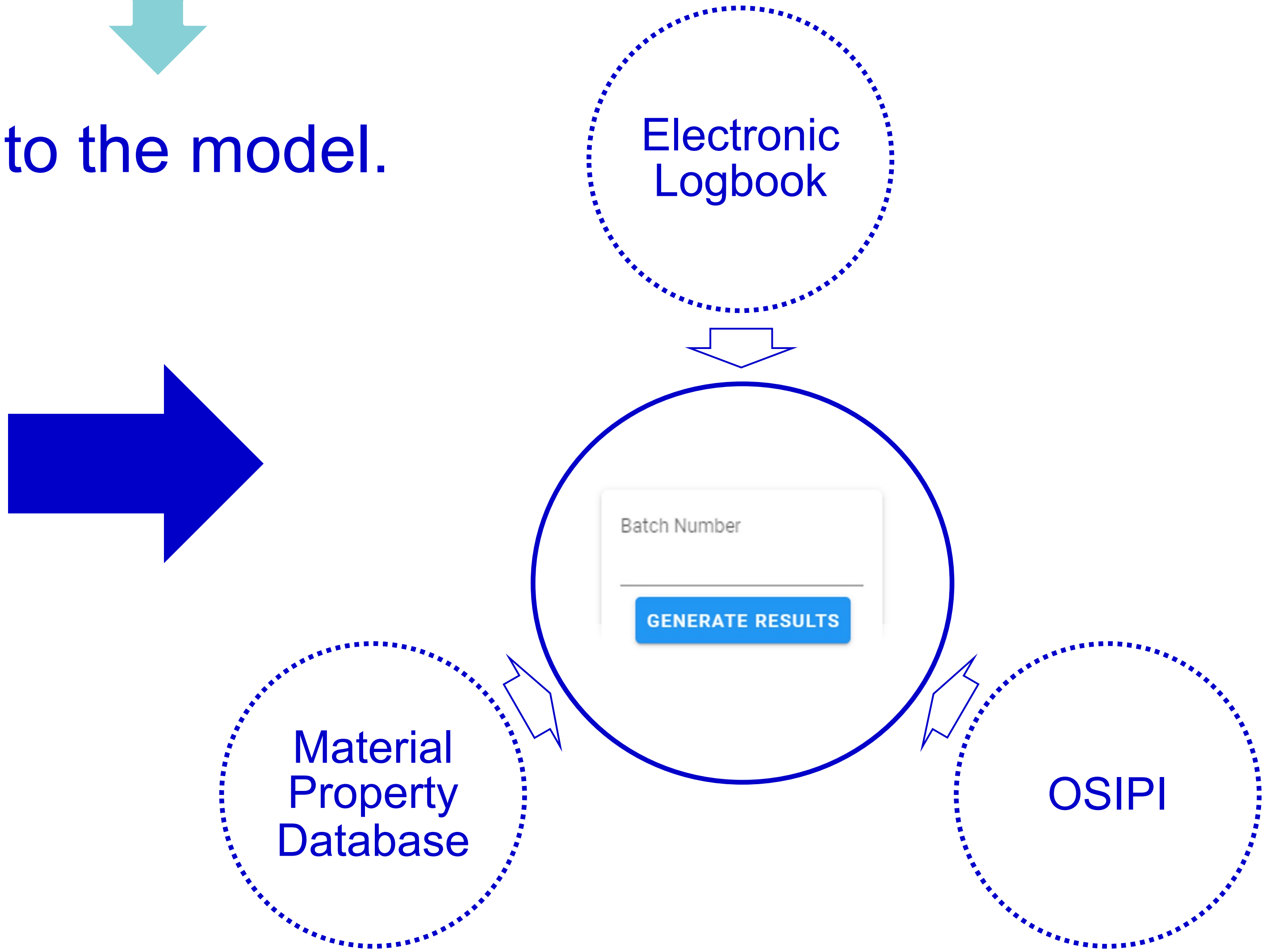
Available Similarity Index Contributors
Particle Size Distribution
Formulation Type (MST x.0)
Drug Load
True Density
Recency

Similarity-Informed Comparison To Historical Data

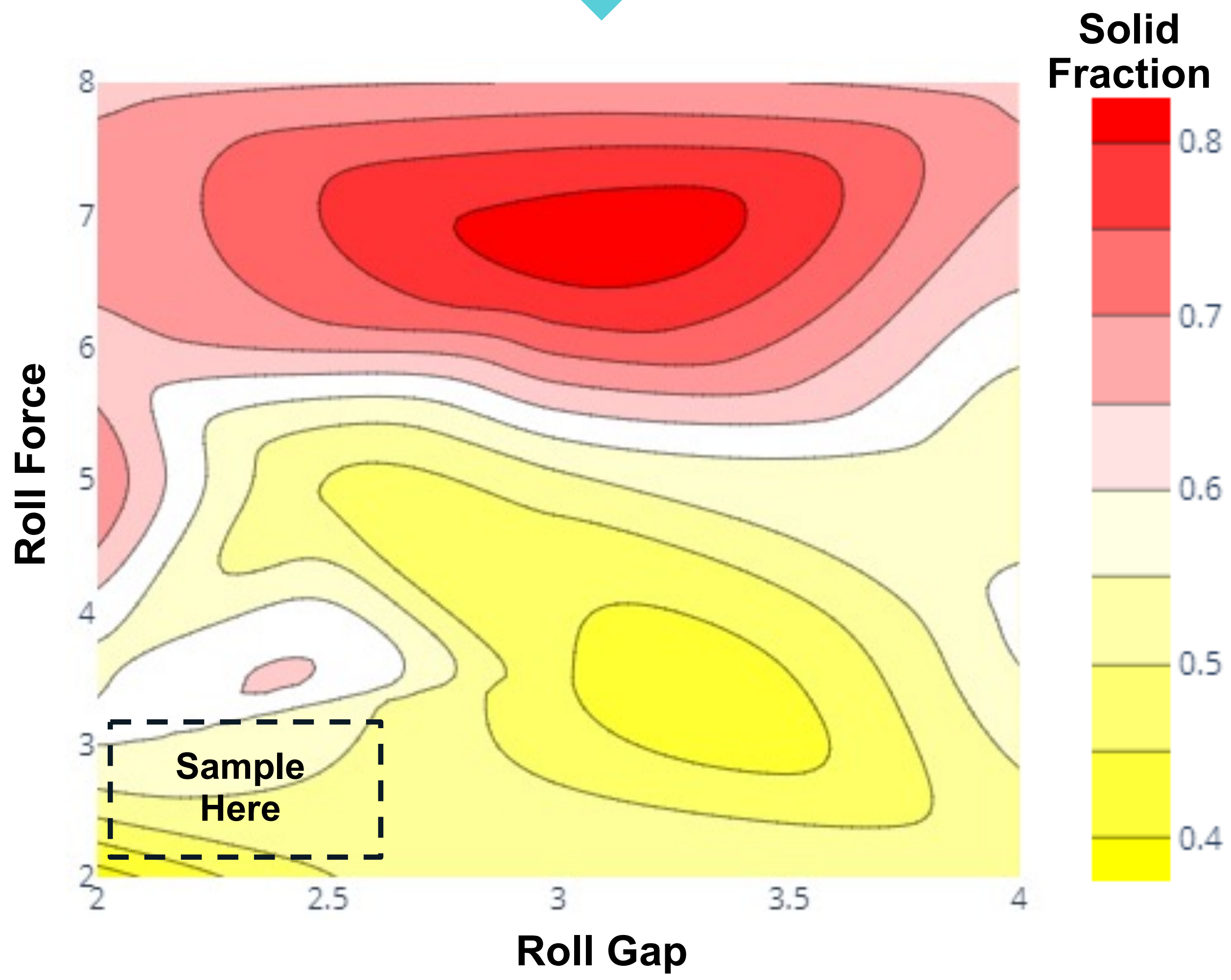
Steps

1) A new product is entered into the model.

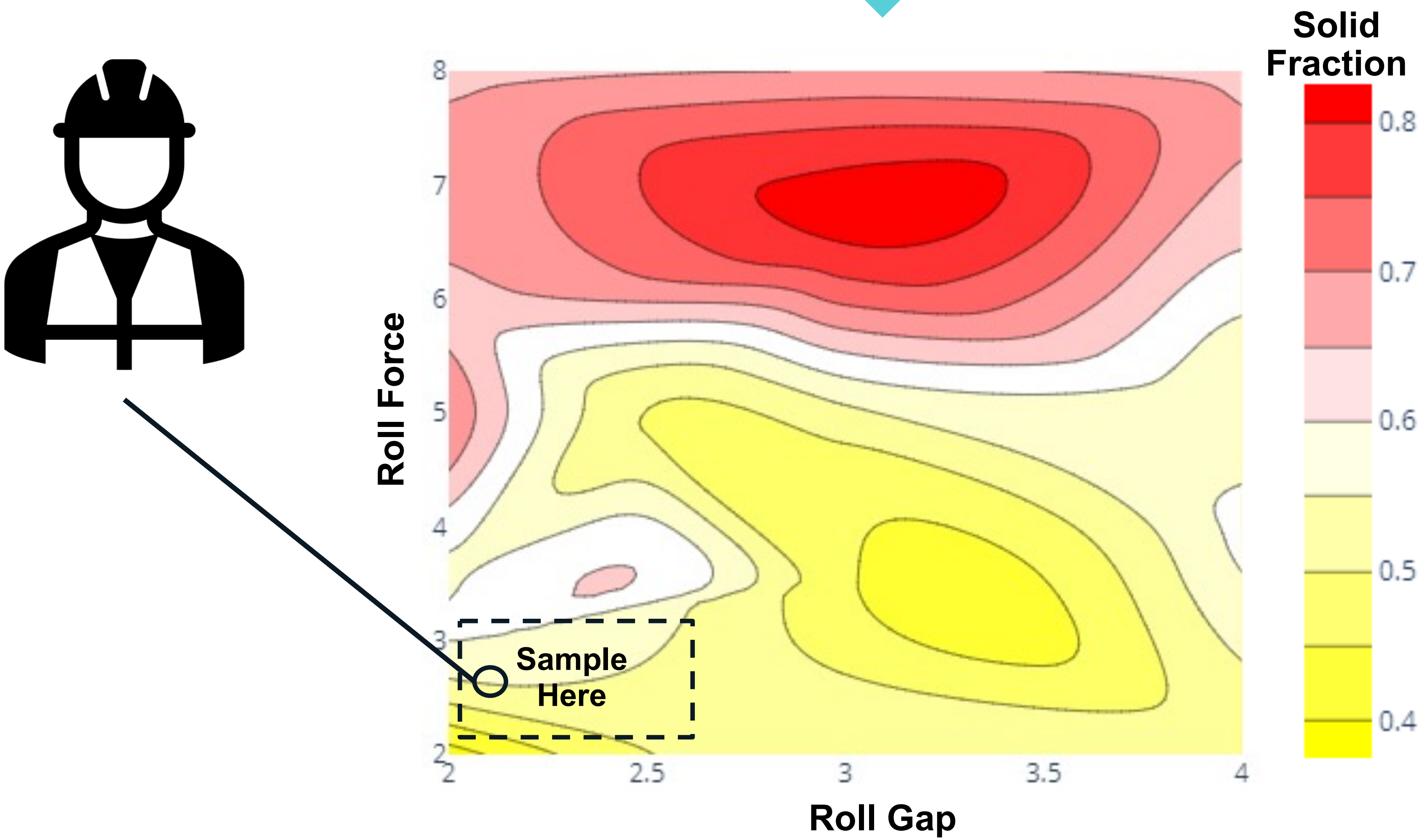




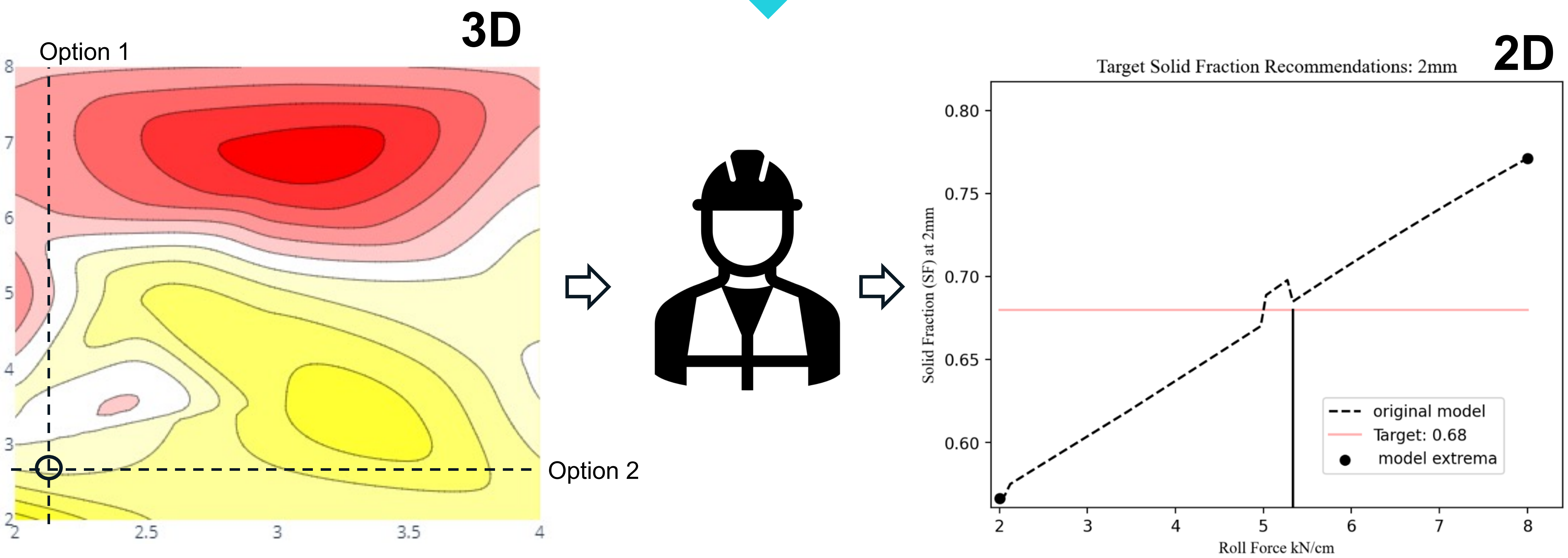
Pre-Sample Prediction



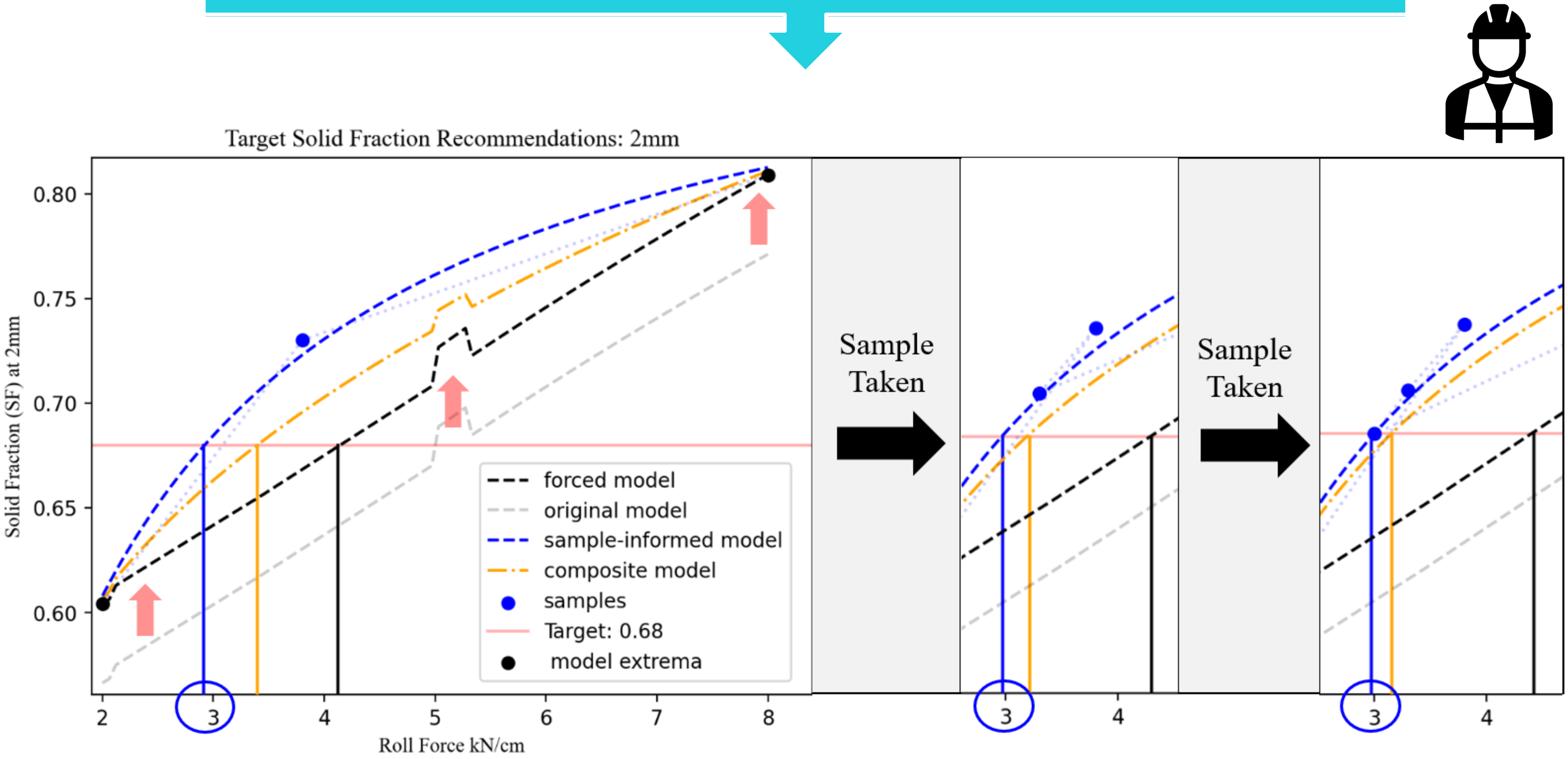
Pre-Sample Prediction



Sample-Informed Regression



Sample-Informed Regression

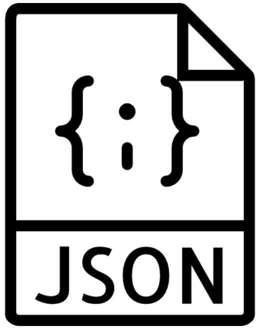


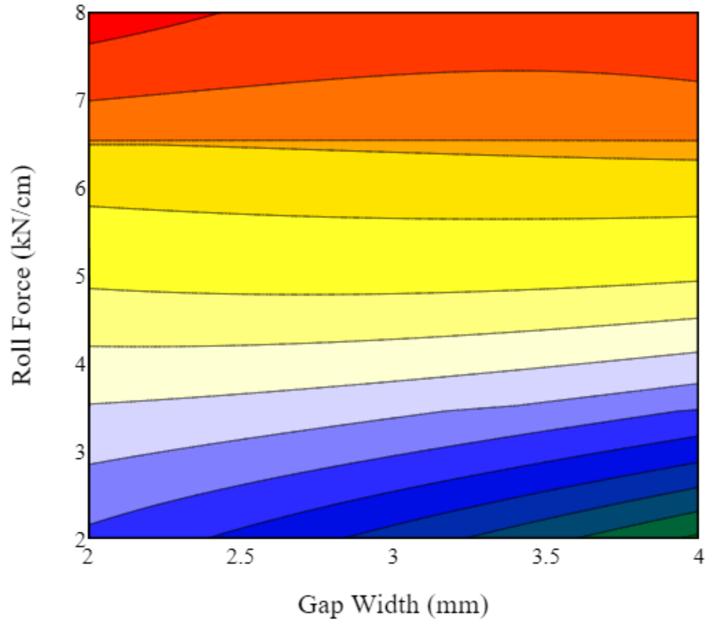
Sample-Informed Regression

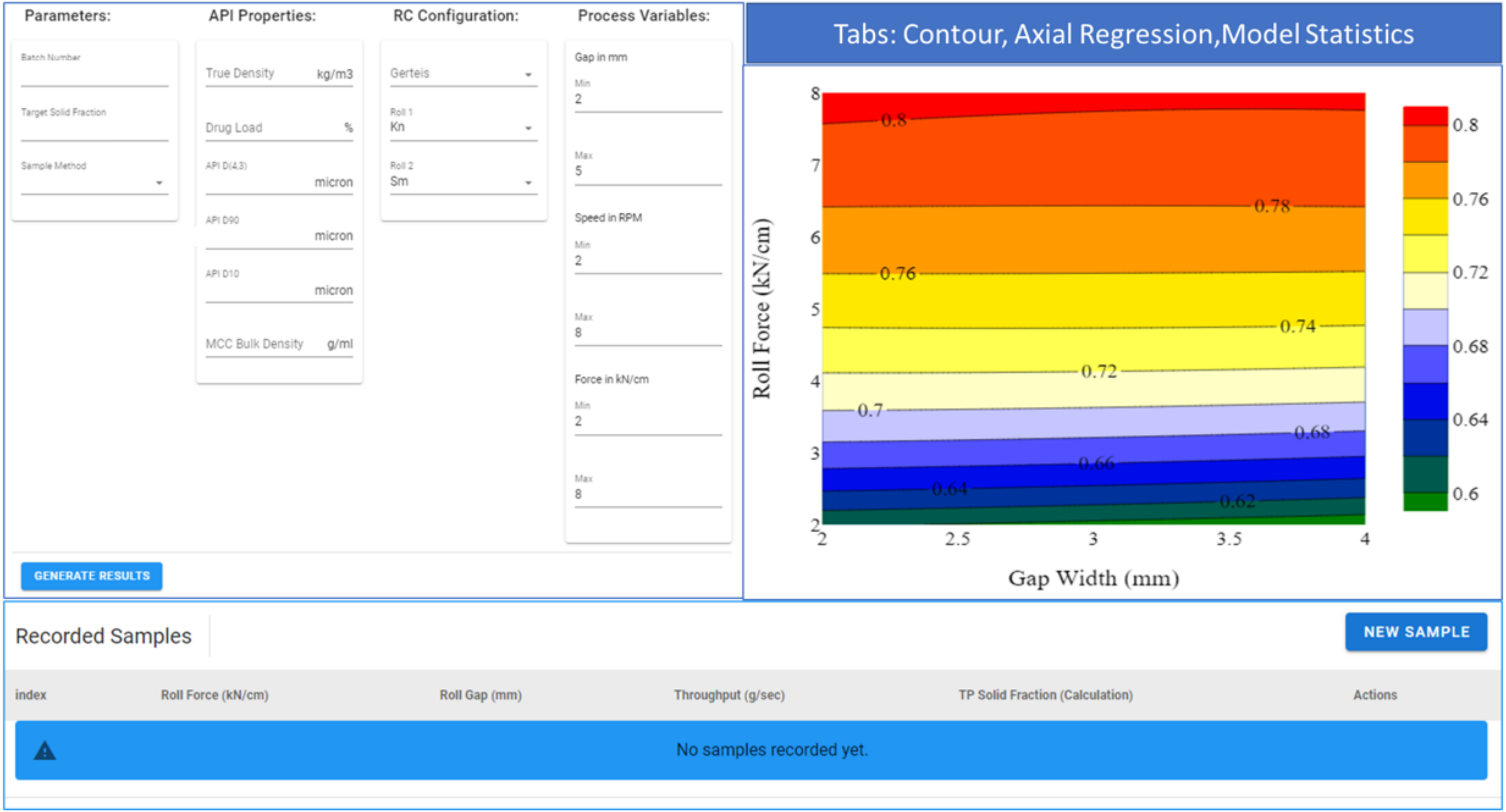
Recorded Samples

NEW SAMPLE

index	Roll Force (kN/cm)	Roll Gap (mm)	Throughput (g/sec)	Solid Fraction (Calculation)	Actions
0	3.5	2		0.66	
1	3.0	2.0		0.63	
2	3.0	2.0		0.63	
3	3.0	2.0		0.63	



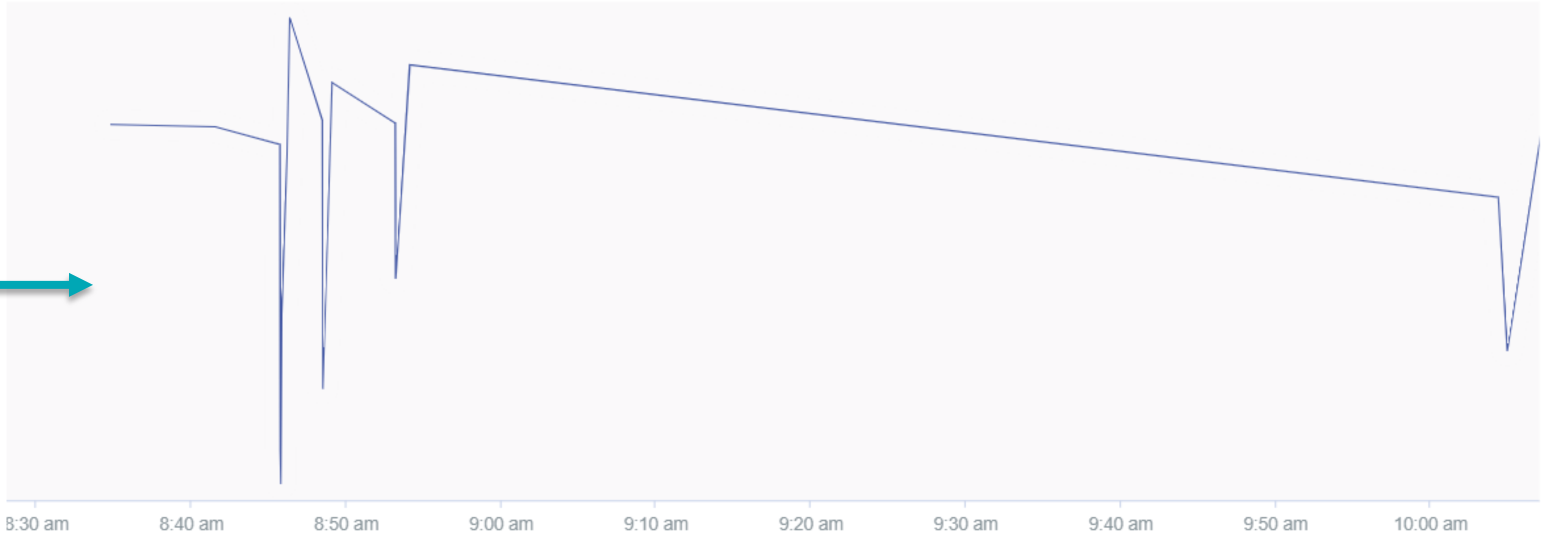


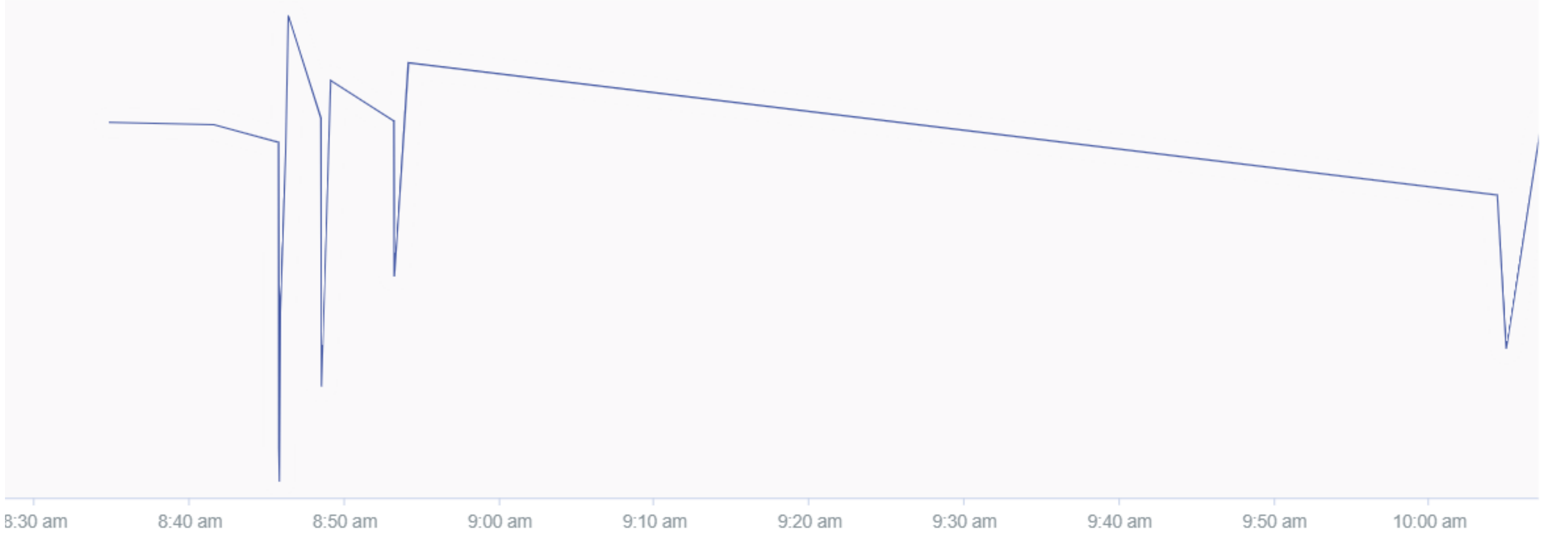

Parameters:
Batch Number
Target Solid Fraction
Sample Method
API Properties:
True Density kg/m3
Drug Load %
API D(4,3) micron
API D90 micron
API D10 micron
MCC Bulk Density g/ml
RC Configuration:
Gerteis
Roll 1
Kn
Roll 2
Sm
Process Variables:
Gap in mm
Min
2
Max
5
Speed in RPM
Min
2
Max
8
Force in kN/cm
Min
2
Max
8
GENERATE RESULTS
Tabs: Contour, Axial Regression,Model Statistics
Roll Force (kN/cm)
Gap Width (mm)
0.8
0.78
0.76
0.74
0.72
0.7
0.68
0.66
0.64
0.62
0.6
Recorded Samples
NEW SAMPLE
index
Roll Force (kN/cm)
Roll Gap (mm)
Throughput (g/sec)
TP Solid Fraction (Calculation)
Actions
No samples recorded yet.

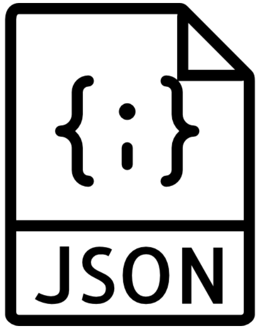
Recorded Samples

NEW SAMPLE

index	Roll Force (kN/cm)	Roll Gap (mm)	Throughput (g/sec)	Solid Fraction (Calculation)	Actions
0	3.5	2		0.66	
1	3.0	2.0		0.63	
2	3.0	2.0		0.63	
3	3.0	2.0		0.63	




8:40 am
8:50 am
9:00 am
9:10 am
9:20 am
9:30 am
9:40 am
9:50 am
10:00 am


JSON

Material-Sparing Tablets

Compaction

Compression

Material-Sparing Tablets

Compaction

Densification

Compressive Forces

Compression

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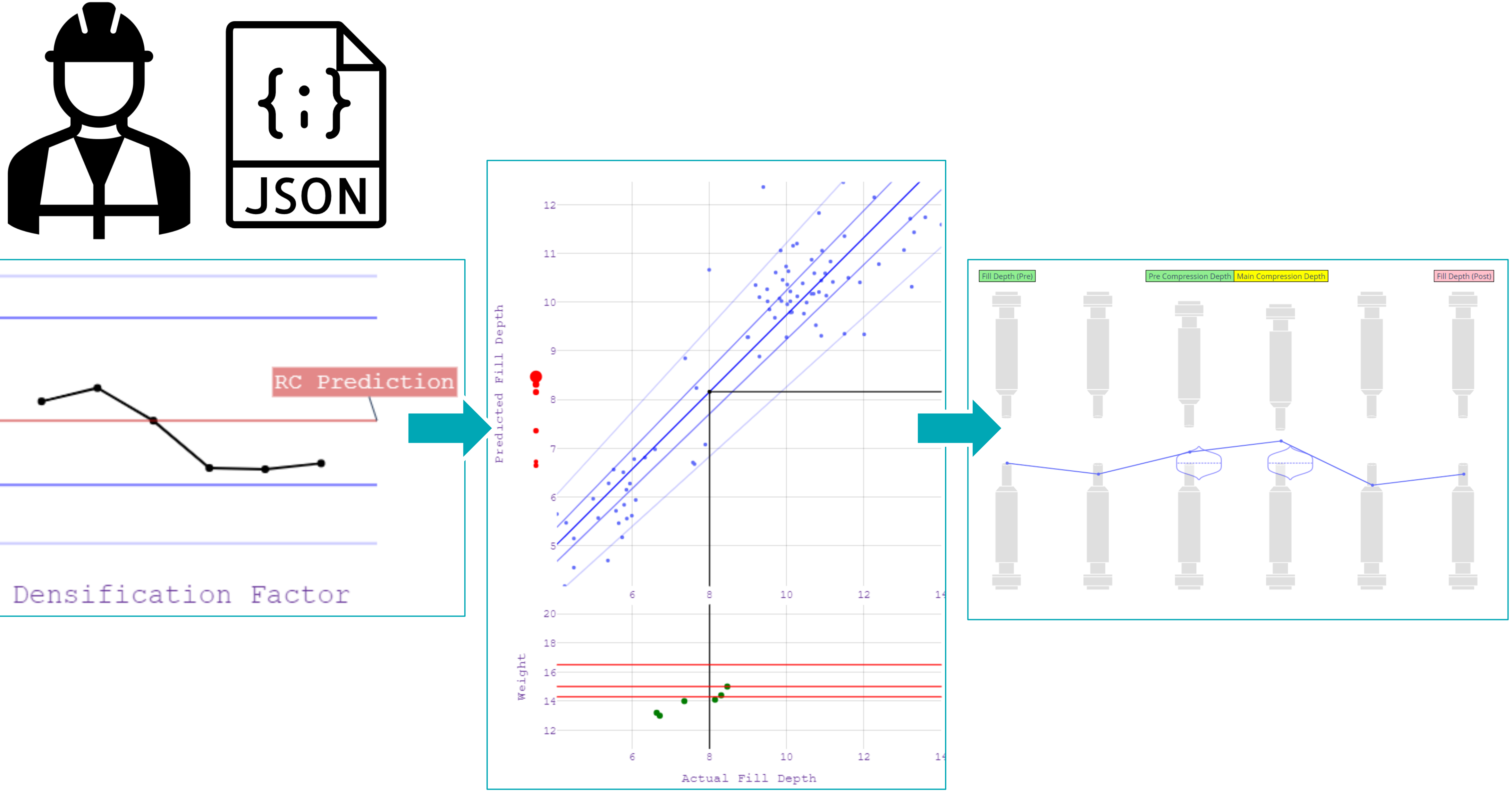
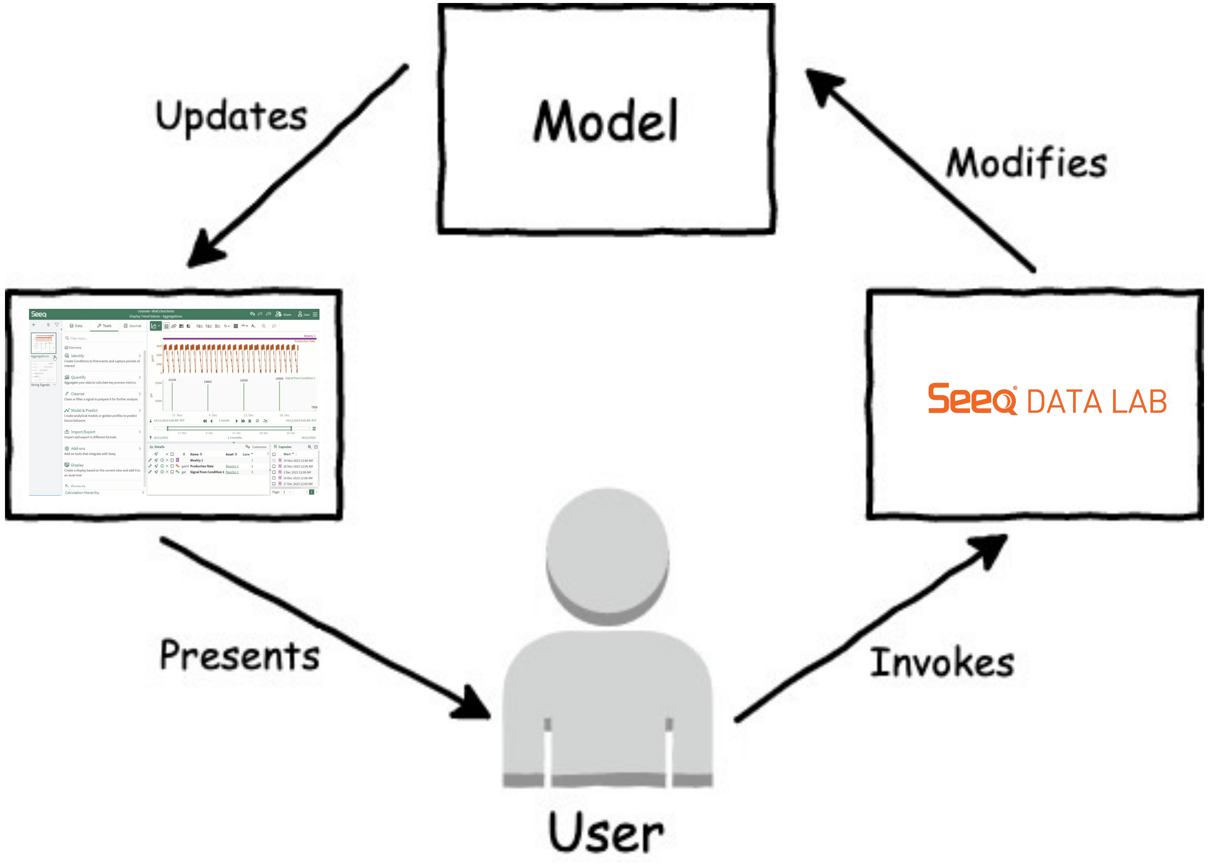

JSON
RC Prediction
Densification Factor
Predicted Fill Depth
Weight
Actual Fill Depth
Fill Depth (Pre)
Pre Compression Depth
Main Compression Depth
Fill Depth (Post)

Seeq® DATA LAB



Key Benefits of Linking Process Models

Stronger Process Control

Shorter Startup Time, Faster Time To Completion

Lower Material Losses