



PI System for Academic Research in Continuous Pharmaceutical Manufacturing

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C-SOPS

PURDUE
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Vision



Science and risk based manufacturing for improved patient reach & healthcare supply

Goal

Real-time release testing in oral solid dose continuous manufacturing systems

Talk Agenda



Continuous Pharmaceutical Manufacturing

Role of PI System in CM Research & Education

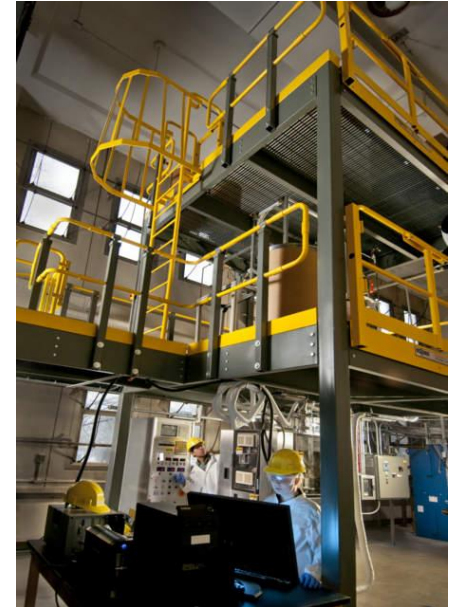
C-SOPS



C-SOPS is the sandbox where academia, industry, and regulators meet (virtually) to develop and refine the next generation of advanced pharmaceutical manufacturing

Highlights:

- Founded in 2006 as NSF ERC-SOPS – Rutgers, Purdue, NJIT, U of PR
- Aided in the development of the continuous version of Janssen's Prezista, first batch to CM conversion
- Funded by FDA to explore CM process/materials; I4.0, Bio modeling
- Working with numerous equipment vendors on characterization, integration, and development.



Current MFG in Pharma (Batch)

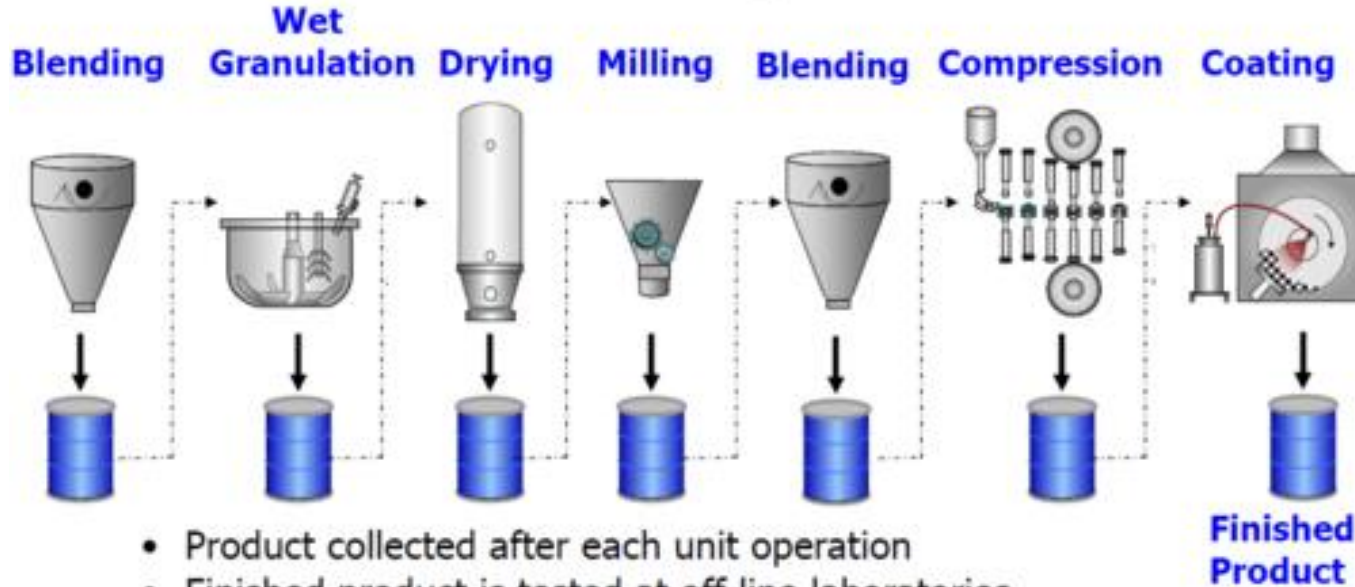
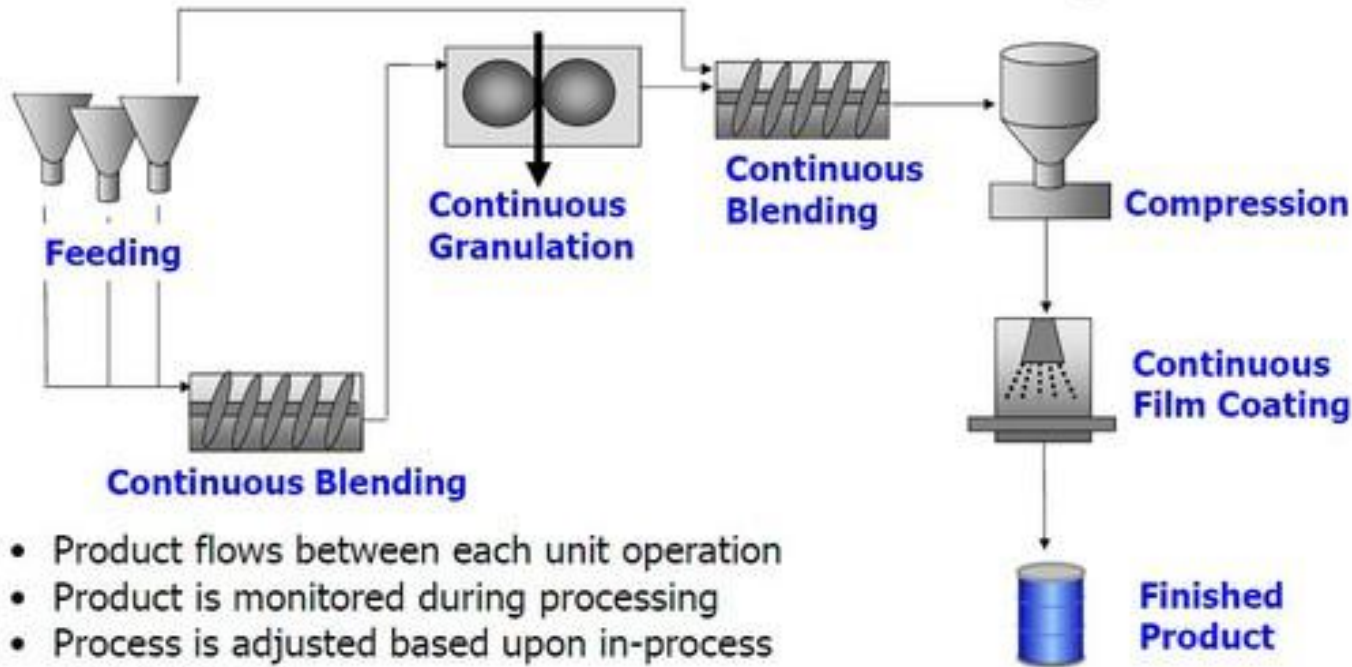


Figure courtesy of the FDA

New MFG in Pharma (Continuous)

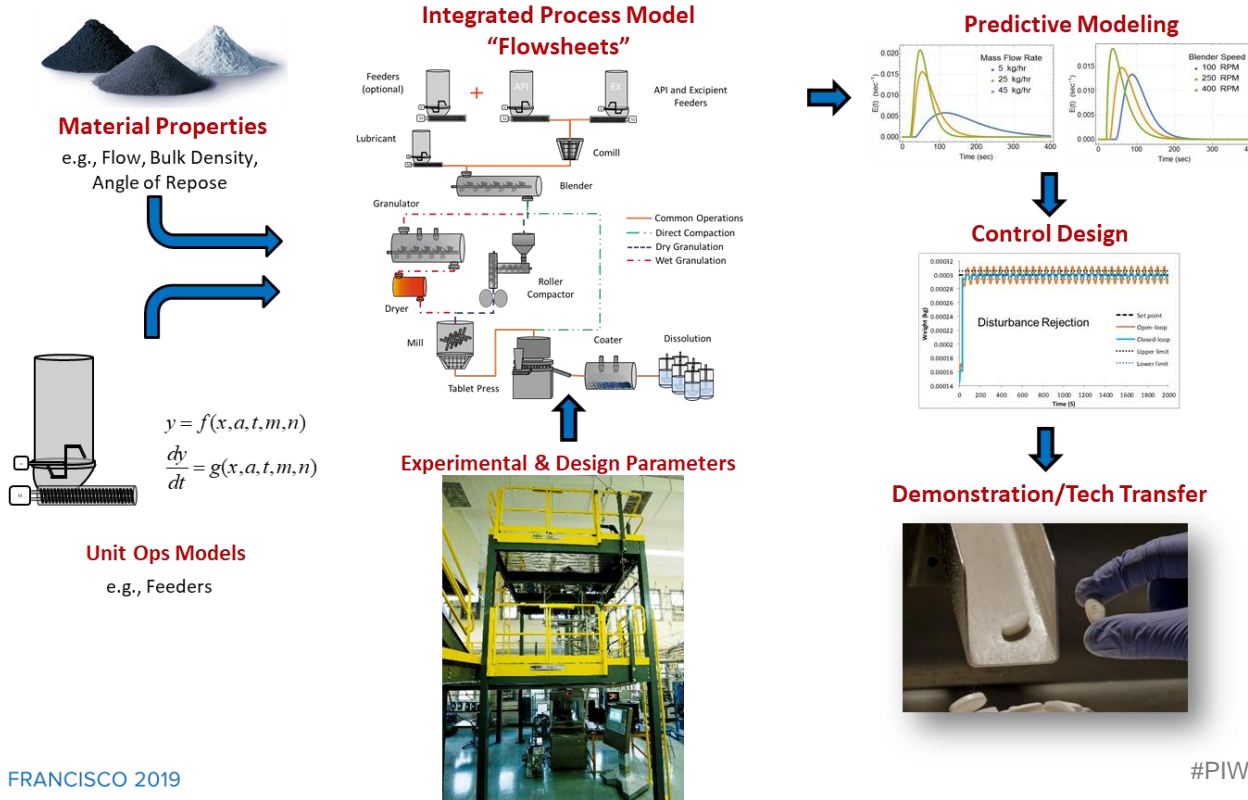


- Product flows between each unit operation
- Product is monitored during processing
- Process is adjusted based upon in-process measurements
- Actual processing time = minutes to hours

Figure courtesy of the FDA

C-SOPS Approach

Solid Dose Advanced Pharmaceutical Manufacturing



CM Solid Dose Adoption Landscape

Regulatory

- FDA actively promoting it (advanced controls and enhanced process understanding required), strong proponent, draft guidance document
- EMA voice has changed from *open to CM* to *encouraging CM*; ETT mindset “big pharma isn’t coming early enough to talk”
- PMDA is starting to provide recommendations (nearly verbatim of C-SOPS Best Practices Document); EMA similar too
- A growing list of regulatory bodies have been exposed to CM and approved processes, including in key markets like Brazil
- ***ICH has decided to take up CM as a 2019 topic!***

CM Solid Dose Adoption Landscape

Branded Pharma

- 2 Vertex, 2 J&J/Janssen, 1 Eli Lilly and 1 Pfizer product(s) already approved in U.S. and other markets
- Above 4 companies have additional products in CM development
- GSK, MSD, Shire/Takeda will all file their first submissions (various markets) within the next few months
- Celgene, Merck KGaA, transitioning from R&D to commercial; working on trials/development with CMOs
- AZ has purchased a commercial GEA system
- BMS revisiting CM using inhouse DC line for development while partnering with a CMO

CM Solid Dose Adoption Landscape

CMOs

- Patheon and Hovione are both now offering solid dose CM contract services

Generics

- Major generic players such as Dr. Reddy's beginning to purchase integrated lines
- In at least one instance pursuing end-to-end CM with integrated drugs substance manufacturing

Vendors

- 5 vendors now offer an integrated solution: GEA, Glatt, Bohle, Powrex, Bosch

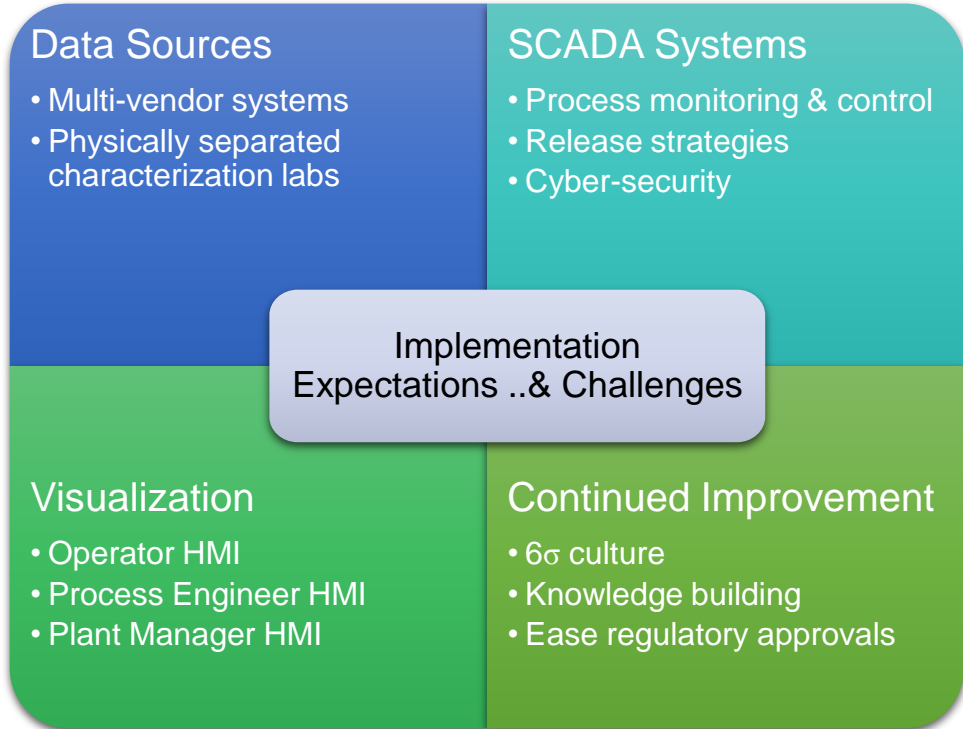
Current focus

Industry 4.0 in pharma development and manufacturing

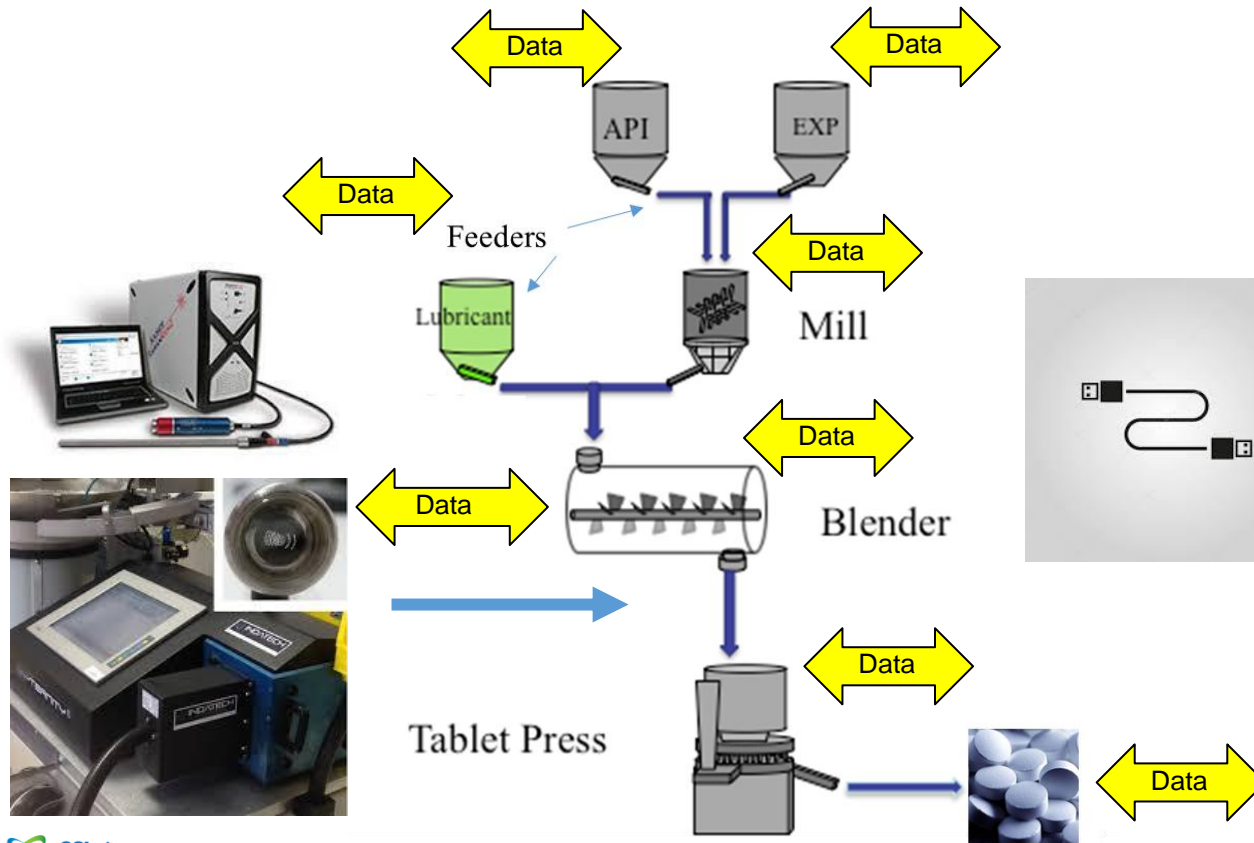
- Leverage interconnected systems, process and product knowledge for real-time release testing, process intensification and safety
- Continued Verification & Improvements
- Material tracking
- Risk assessment
- Visualization



Grant U01FD006487 (2018)

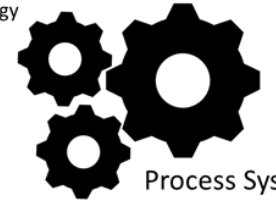


Rutgers Direct Compression (DC) CM Line



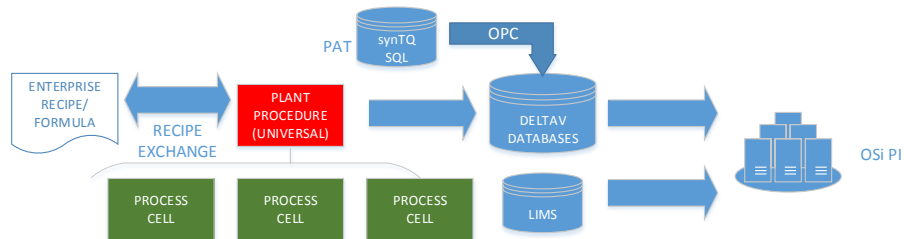
Material Handling
Particle Technology

Process
Analyzers
In-line, At-line &
Offline

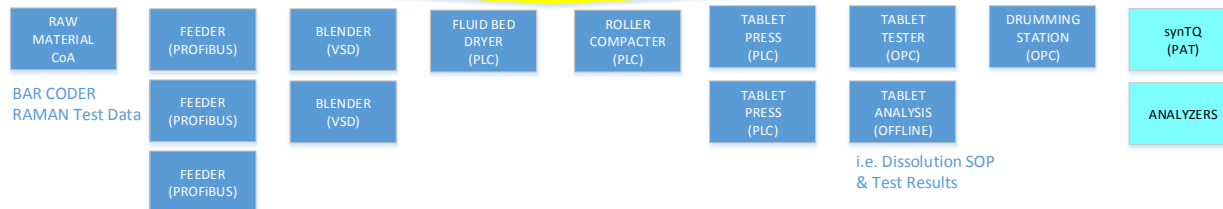
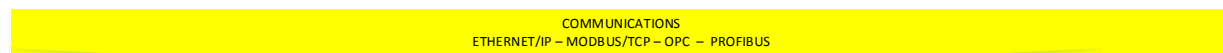
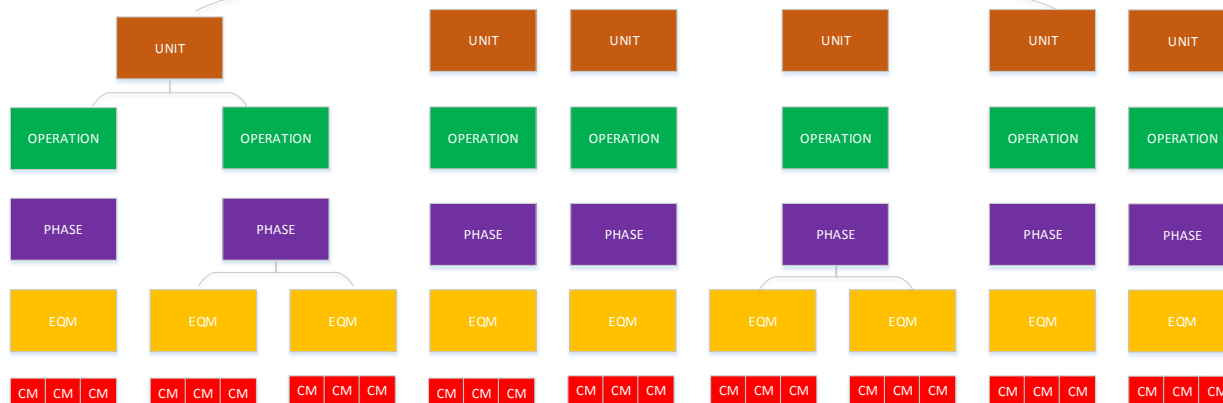


Process Systems
Engineering

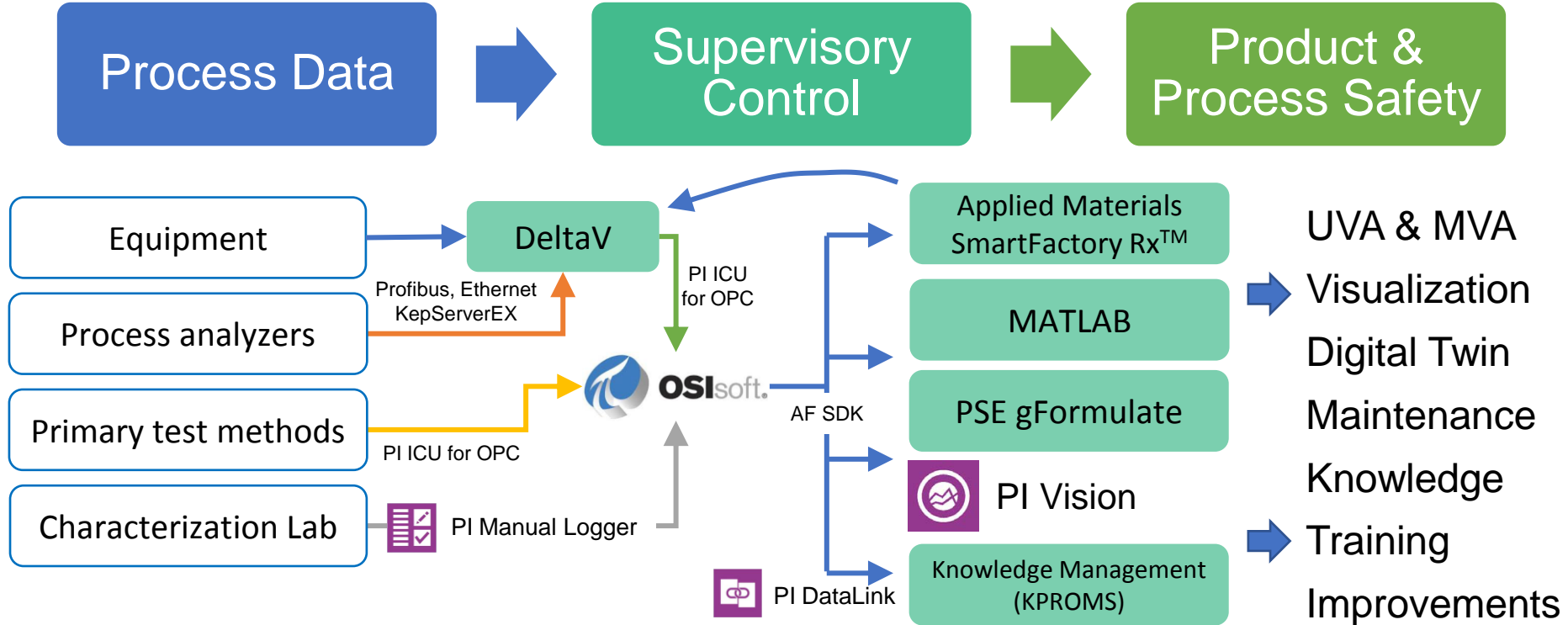




Rutgers Line Network Infrastructure

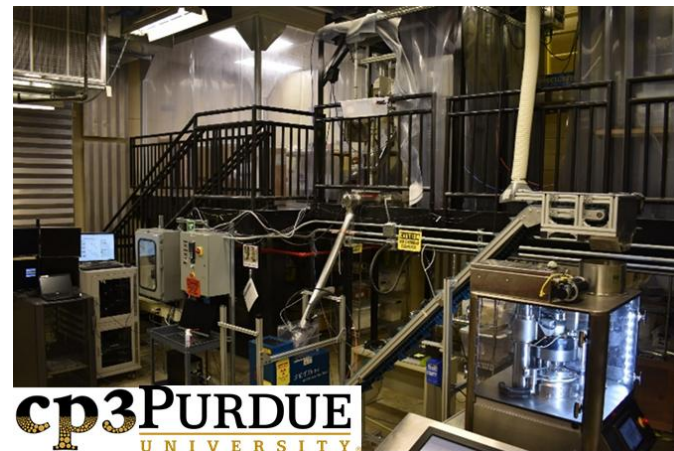


Process operations implementation





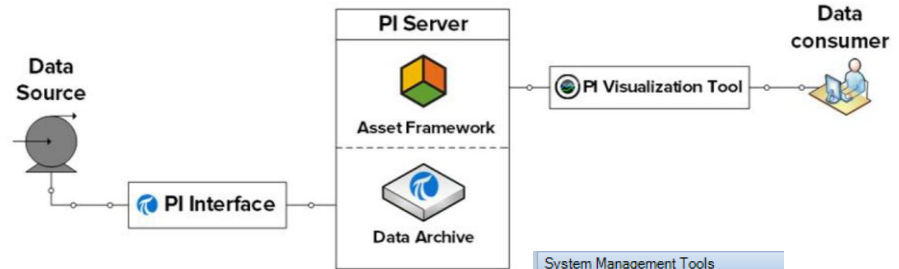
- Davidson School of Chemical Engineering
- Center for Particulate Products & Processes (Purdue CP3)
 - Solids processing research and education
 - Pharma, consumer products, agriculture, chemicals, food, ceramics etc.
 - Solids characterization facility
 - OSD continuous manufacturing pilot plant
- Commissioned PI System in Oct 2018



Role of PI System

Step 1: Get the data!

- PI SMT, PI ICU
 - Archiving – data source, rate of acquisition, data types, precision
 - Control database access
- PI Manual Logger



General	Archive	Classic	Security	System
Name:	CDT158			
Descriptor:	Atmospheric Tower OH Vapor			
Stored Values:	Real-time data	Point Source:	R	
Point Type:	Float32	Digital Set:		
Eng Units:	Float32			
Exdesc:	Float32			
Source Tag:	Int16			
	Int32			
	String			
	Timestamp			
	Raw			

General	Archive	Classic	Security	System	
Typical Value:	5	Zero:	0	Span:	10
Scan	Archiving	Step	Shutdown	Compressing	
<input checked="" type="radio"/> On	<input checked="" type="radio"/> On	<input type="radio"/> On	<input checked="" type="radio"/> On	<input checked="" type="radio"/> On	
<input type="radio"/> Off	<input type="radio"/> Off	<input checked="" type="radio"/> Off	<input type="radio"/> Off	<input type="radio"/> Off	
Exception Deviation		Compression Deviation			
0.01 Eng. Units		0.02 Eng. Units			
Min. Time: 0 0 0 0		Min. Time: 0 0 0 0			
Max. Time: 0 0 10 0		Max. Time: 0 8 0 0			

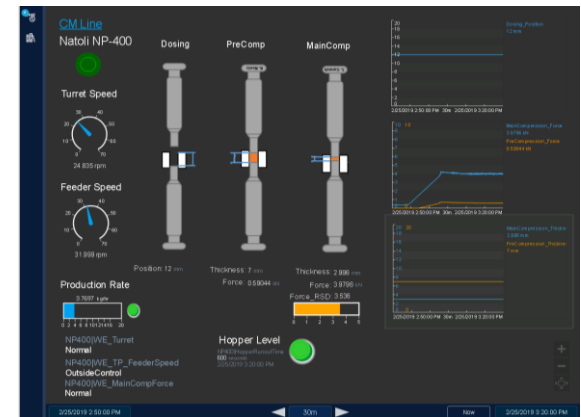
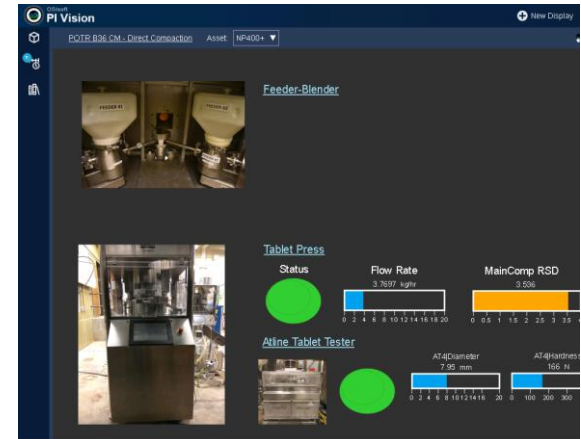
System Management Tools
Search
> Alarms
> Batch
> Data <ul style="list-style-type: none">Archive EditorCurrent ValuesStale and Bad Points
> Interfaces <ul style="list-style-type: none">AutoPointSync ListInterface List
> IT Points
> Operation
> Points <ul style="list-style-type: none">Digital StatesPerformance EquationsPoint BuilderPoint ClassesPoint Source TableTotalizers
> Security <ul style="list-style-type: none">Database SecurityFirewallIdentities, Users, & GroupsMappings & TrustsSecurity Settings

Role of PI System

Step 2: Contextualize the data

- PI Asset Framework
 - Map assets, define events
- PI Vision – real-time visualization

The screenshot displays the PI Asset Framework (PI AF) interface. On the left, the 'Elements' tree shows a hierarchy starting with 'PotterB36', followed by 'Blender 1', 'Blender 2', 'Feeder 1', 'Feeder 2', 'InterFaces', 'LubricantFeeder', 'MTBalance', 'MultiEye_Head1', 'MultiEye_Head2', 'NP400', 'WP120_Old', and 'X-ray_MassFlow'. Below this is an 'Element Searches' section. The main panel shows the 'NP400' asset with various categories like 'Category: Cpk', 'Category: Equipment Information', 'Category: Equipment Status Data', 'Category: Individual Stations', and 'Category: Process Data'. The 'Process Data' category is expanded, showing a list of attributes such as 'Dosing_Position', 'FeederSpeed', 'MainCompression_CalculatedRSD', 'MainCompression_Force', 'MainCompression_RSD', 'MainCompression_SDev', 'MainCompression_Thickness', 'PreCompression_Force', 'PreCompression_Thickness', 'StationPos_Dosing', 'StationPos_Ejection', 'StationPos_LastTabRejected', 'StationPos_MainCompression', 'StationPos_PreComp', 'Turret_Speed', and 'TurretCommand_TDM'. A 'Functions' panel on the right lists various functions like 'Time Series Value Statistics', 'All', 'Array Operations', 'Date and Time', 'Event Frame Properties', 'Logical', 'Math', 'Operators', 'PI Data Archive Digital States', 'Point Attributes', 'Search and Retrieval', 'Statistical', 'Status', 'Stream', 'String', 'Time Series Value Statistics', 'Cov', 'EventCount', 'LinReg', 'PctGood', 'Range', 'StDev', 'TagAvg', 'TagMax', 'TagMean', 'TagMin', and 'TagTot'.



Role of PI System

Step 3: Interface with data consumers for advanced analytics

- AF SDK
 - MATLAB
 - Applied SmartFactory Rx™
- PI DataLink in Excel
 - Experimental records
 - Testing new analyses
 - Collaborations, education
- Consistent tag naming helps!

%add OSISOFT .NET references to be able to use them

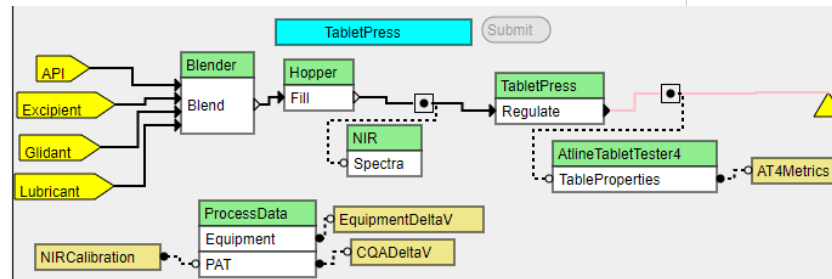
```
afsdk = NET.addAssembly('OSISOFT.AFSDK');  
import OSISOFT.AF.*;  
import OSISOFT.AF.Asset.*;  
import OSISOFT.AF.Time.*;  
import OSISOFT.AF.Data.*;  
import OSISOFT.AF.PI.*;  
import System.*
```

```
% connect to Purdue PI AF server  
piSystems = OSISOFT.AF.PISystems;  
fprintf('Connecting and refreshing')
```

```
af_svr = piSystems.Item('██████████');  
af_db = af_svr.Databases.Item('██████████');
```

```
% confirm database connection  
af_db.Refresh();  
fprintf('\nConnected\n');
```

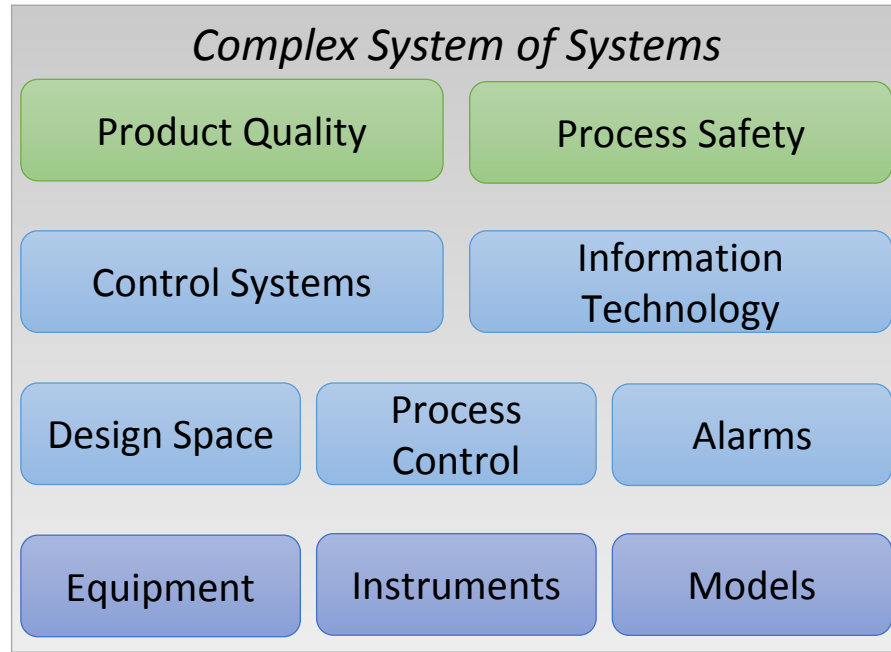
	G	H	I	J	K	L	M	N	O
g_PcFeederSpMainCom	MainCom	MainCom	MainCom	MainCom	MainCom	MainCom	MainCom	MainCom	MainCom
12	6.486851	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.507269	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.527687	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.548105	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.568523	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.588941	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.609359	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.629777	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.650195	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.670613	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.691031	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015
12	6.711449	0.370049	0.452926	0.454262	0.404299	0.450471	0.393602	0.415749	0.400015



Knowledge Provenance Mgmt. System (HUBZero)

QbD to operational excellence

Reliable process operations in OSD CM



What if... sensors fail?

Failure/gross error causes:
Communication, fouling, orientation,
calibration, device life

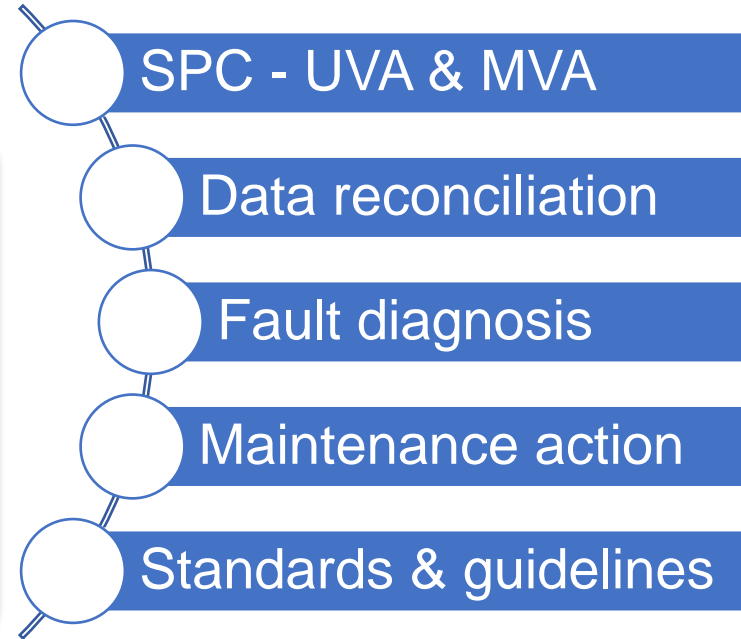
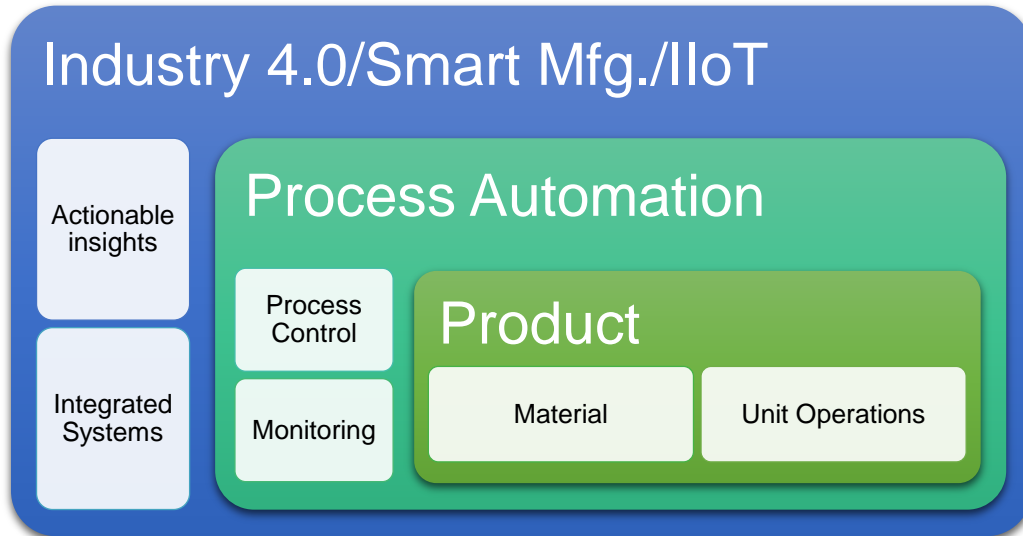
Impacts Quality & Consumer Reach

- Increased offline quality testing
- Diminished competitive advantage
- Limits/Questions use of technology

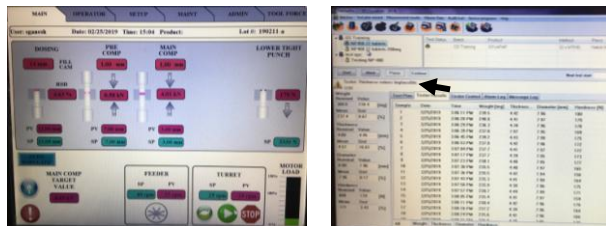
QbD to operational excellence

Reliable process monitoring in OSD CM

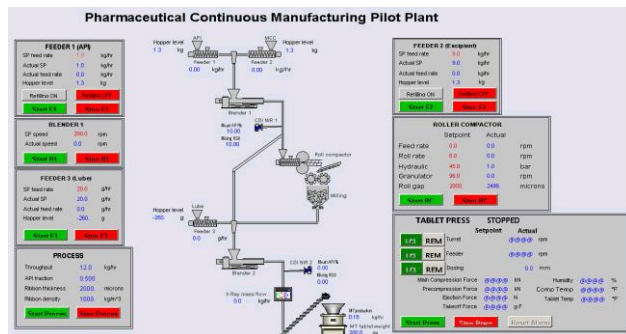
Objective: Condition-based maintenance for sensor network reliability in OSD CM



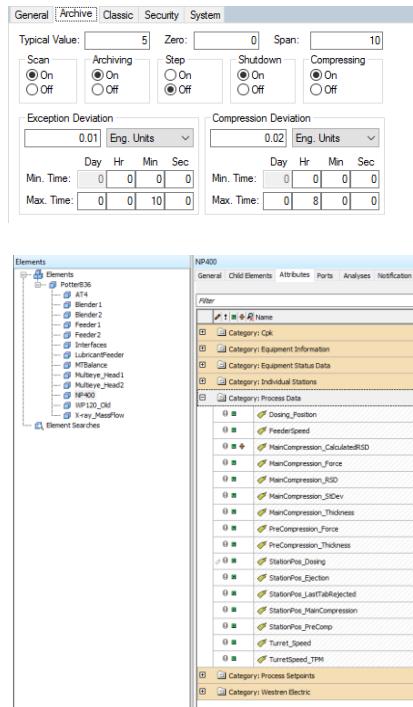
From device data to supervisory strategies



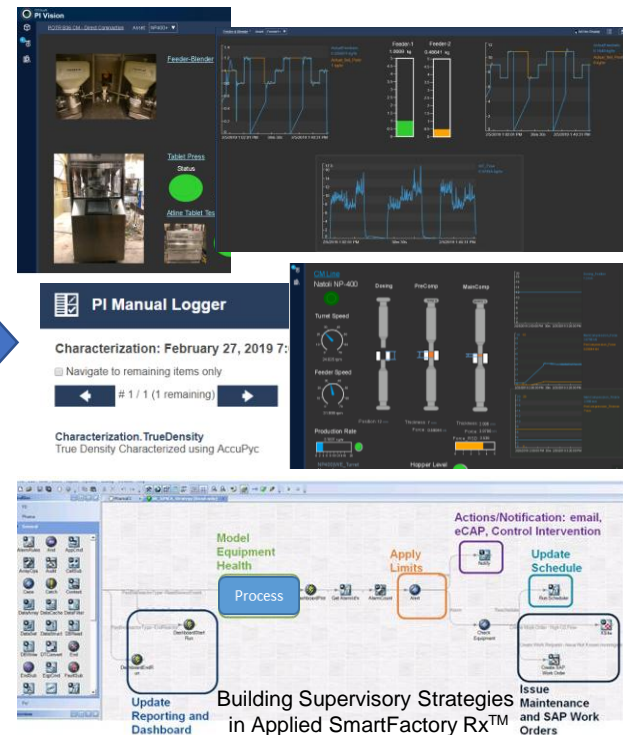
Individual equipment & sensors



Operations configuration



Setup PI System



Visualization & additional systems

Setup, training and continued learning

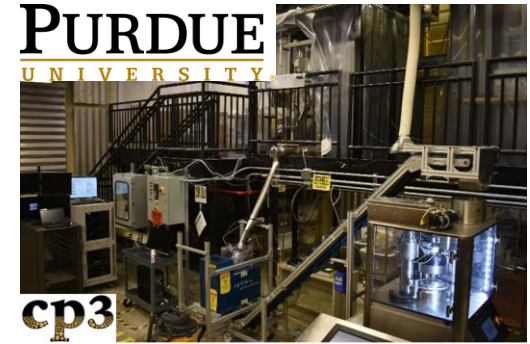
Resources for independent and intuitive learning

- Understand your data
- YouTube
- PI Square training modules
- Documentation
- PI World presentations
- Tech support
- White papers

The image displays two screenshots of OSiSoft's online resources. The top screenshot is the 'PI Square' website, which serves as a community hub. It features a navigation bar with links to Home, News, Spaces, People, Ideas, and Content. Below the navigation bar are three main categories: 'All Things PI' (green), 'PI Developers Club' (orange), and 'Online Courses' (purple). The main content area includes a search bar, a 'PI PRODUCTS' section with icons for PI Server, PI Visualization, PI Interfaces and Connectors, PI Developer Technologies, PI Cloud Connect, and PI Integrators. There is also a 'NEED HELP?' section with a 'Post a Question' button and a 'QUICK LINKS' section with links to 'PI Square Groups' and 'AF Community Library'. The bottom screenshot is the 'OSiSoft Learning' and 'OSiSoft Tech Support' page. It features a navigation bar with links to HOME, VIDEOS, PLAYLISTS, and COMMUNITY. Below the navigation bar is a section for 'Asset Framework - Explore metadata, add analytics, and get more'. The main content area is divided into two columns. The left column contains video thumbnails and titles for 'Getting Started with Asset Framework', 'Asset Analytics with PI AF', and 'PI AF (Asset Framework)'. The right column contains a 'Things to Do' section with links to 'Generate a License File', 'Open a New Support Case', 'Download Software', 'Update My Profile', and 'Try PI DevClub for free'. Below this is a table with three columns of links: 'My Support', 'Contact Us', 'Resources', 'Downloads', and 'Products'. The table contains links to various resources, including 'PI System Roadmap', 'PI System Cyber Security', 'PI Square Community', 'Learning Videos', 'Live Library', 'System Management Resources', 'My Downloads', 'All Downloads', 'My Download History', 'PI Server', 'Visualization', 'Interfaces and Connectors', 'Integrators', 'PI Cloud Connect', and 'Developer Technologies'.

Purdue University Center for Particulate Products and Processes (CP3)

Process analytics research and education using PI System in OSD CM & solids processing pilot plant



CHALLENGE

Systems Integration & Operational reliability for real-time release in OSD CM systems

- Product quality tracking & release
- Manage systemic risks – sensor & equipment failure, cybersecurity

SOLUTION

PI System commissioned for data integration & enabling advanced analytics

- ICU, Manual Logger, Vision, Asset Analytics, Event Frames, DataLink
- AF SDK used to interface with Matlab, AMAT SmartFactory Rx™

RESULTS

Insights for predictive analytics - supervisory control, release strategies, maintenance etc.

- Advancing pharmaceutical manufacturing
- Data science research & education using real-world examples

Acknowledgement

- OSIssoft Academic Team - Mike Mihuc, Erica Trump
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- Our supporters and partners, and the community interactions

PI System in Continuous Pharmaceutical Manufacturing



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Questions?

Please wait for
the **microphone**

State your
name & company



Please remember

TO DOWNLOAD
APP, SEARCH
OSISOFT



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