



Digitalizing Recipe Management to Accelerate Tech Transfers

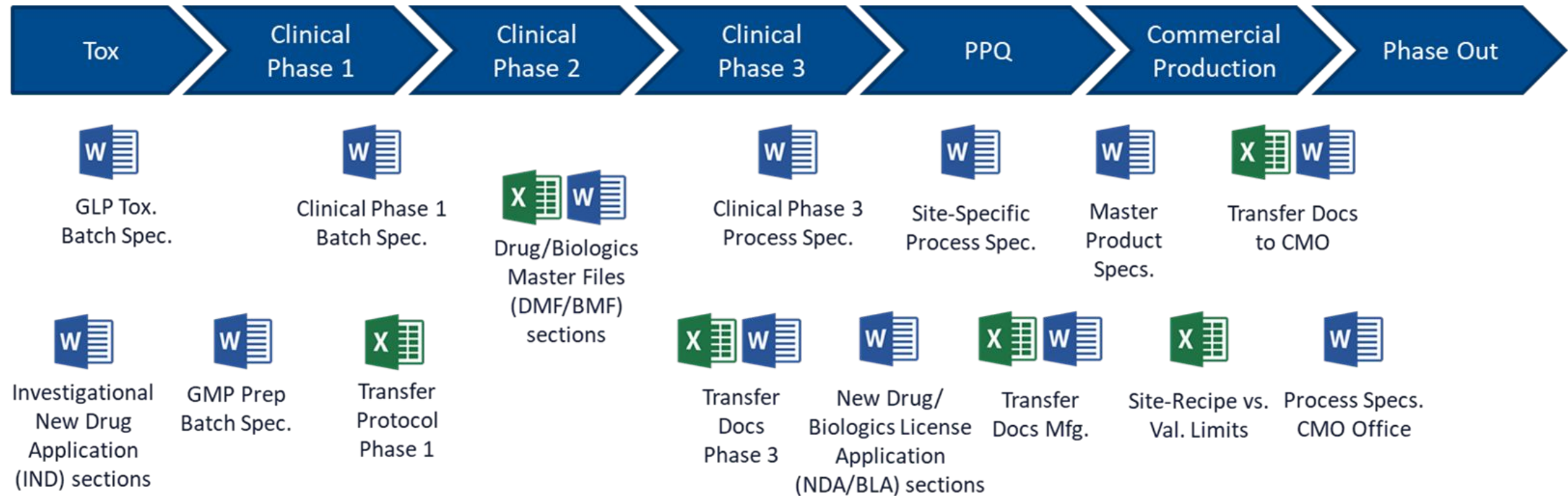
Translating Development Data into Manufacturing



Agenda

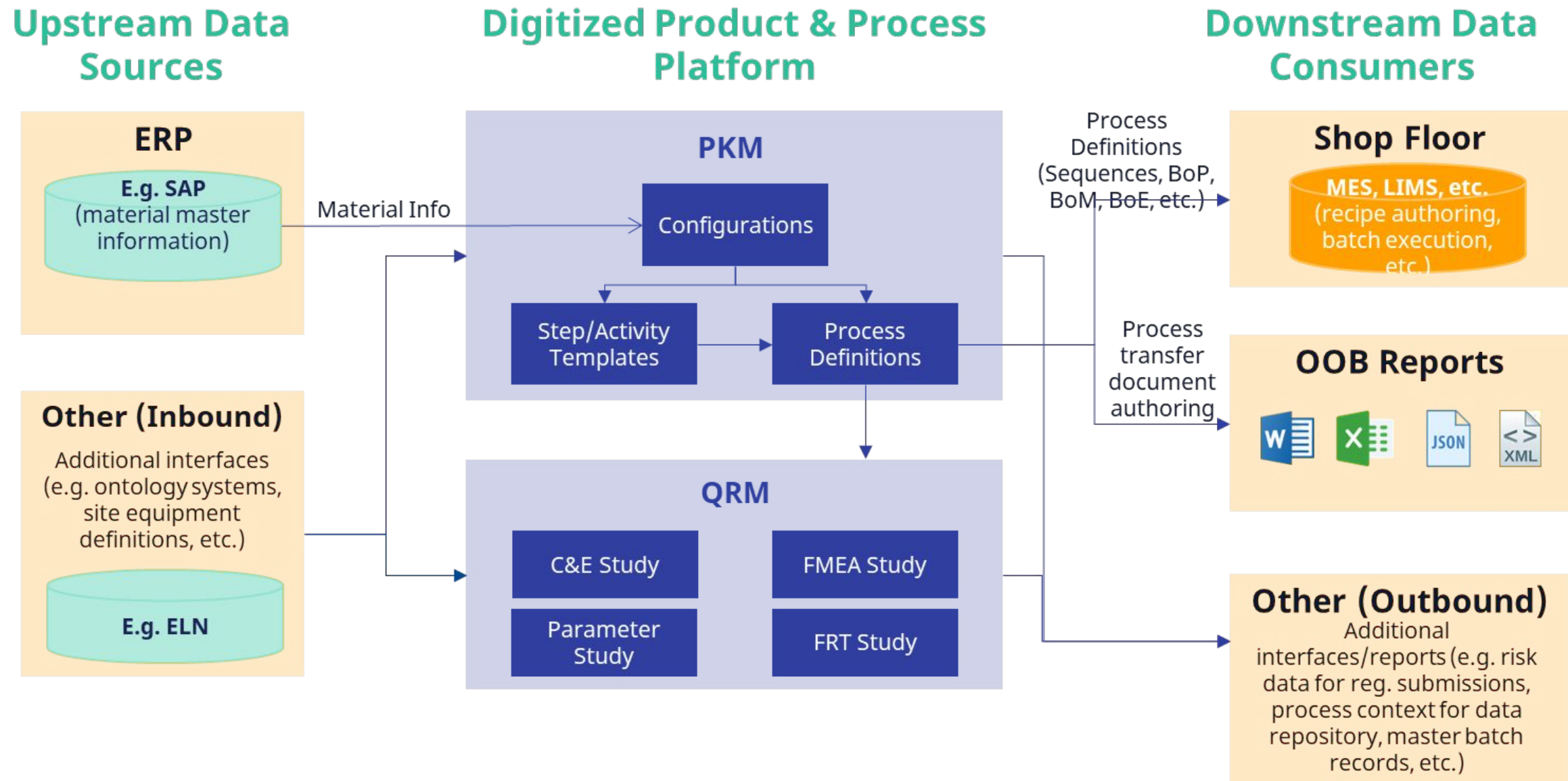
- 1 Recipe Lifecycle: Document-led to Data-led Model
- 2 Digital Tech Transfer: Boiling the Ocean
- 3 Connecting Process Knowledge to Execution Systems
- 4 One-click Tech Transfer Success Stories

Document-led Model – Disconnected Data Silos



What if all of this could be managed in one electronic format?

Data-led Model – Single Source of Truth

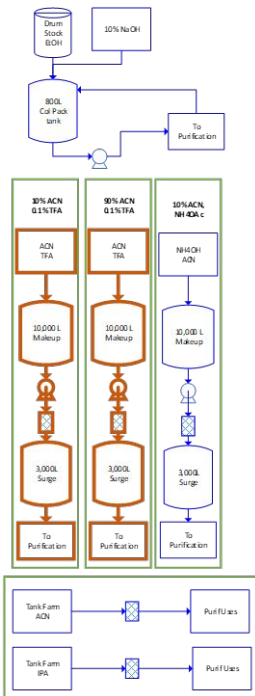


Developing Standardized Model for a Product is a Key Early Step

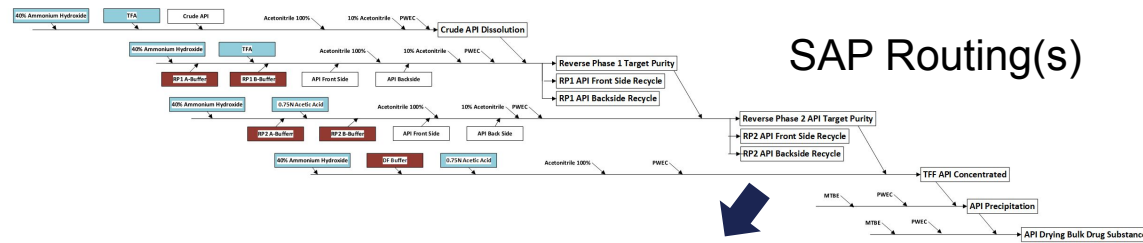
Process Narrative

Process Flow Chart

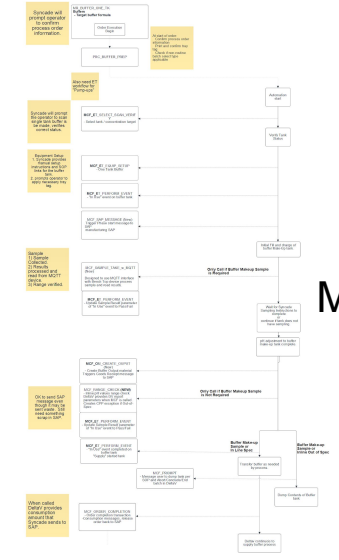
Step #	Process Flow	Control Parameter	Parameter Target	Normal Operating Range (NOR)	Acceptable Range (AR)/ Proven Acceptable Range (PAR)	Parameter Type
1		Reversed Phase 1 A-Buffer Make-up 0.1% TFA, 10% ACN				
		ACN Content %	10%	8-11%	8-12%	Non-Critical
		TFA Content %	0.10%	0.09-0.11%	0.07-0.13%	Non-Critical



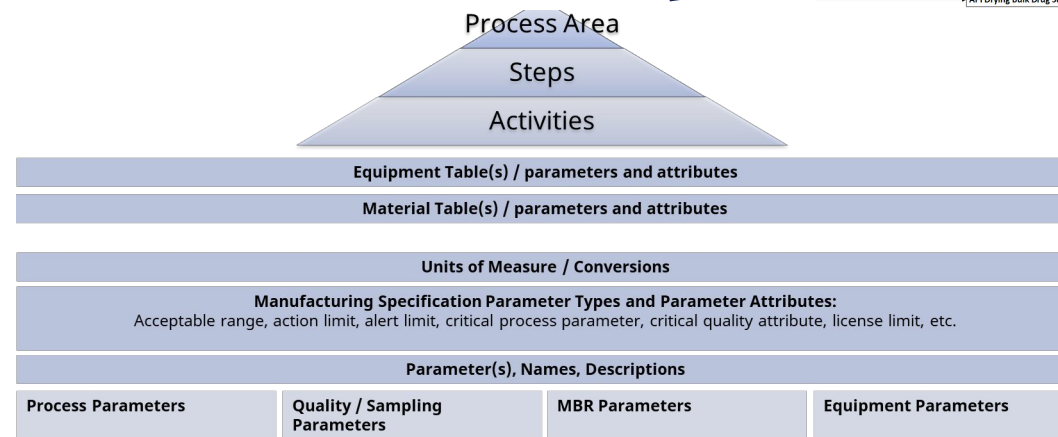
Process Flow Diagrams



SAP Routing(s)



MES Recipe Flow



Standardized Data Model

Process Parameters	Quality / Sampling Parameters	MBR Parameters	Equipment Parameters
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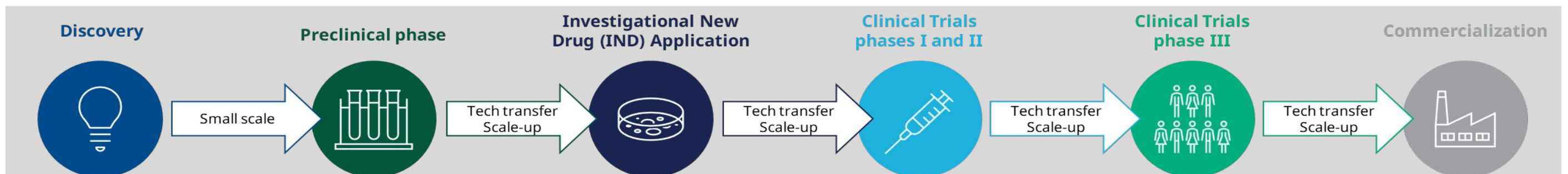
Manufacturing Procedure

Step No.	Parameter Name	Procedure Step	Procedure Step Start/Stop Time	Procedure Step State
Wash				
Temperature Adjust and Mix				
1	Internal Temperature	Adjust the Internal Temperature of Bioreactor to NMT 37 °C, target 36 °C	Start Date: _____ Hrs Stop Date: _____ Hrs	
2	Mix	Mix the contents of 100 L Jacketed Reactor 1 times	Start Date: _____ Hrs Stop Date: _____ Hrs	
Mix 1				
1	Internal Temperature	Adjust the Internal Temperature of 100 L Jacketed Reactor to NLT 35 °C, target 36 °C	Start Date: _____ Hrs Stop Date: _____ Hrs	⚠

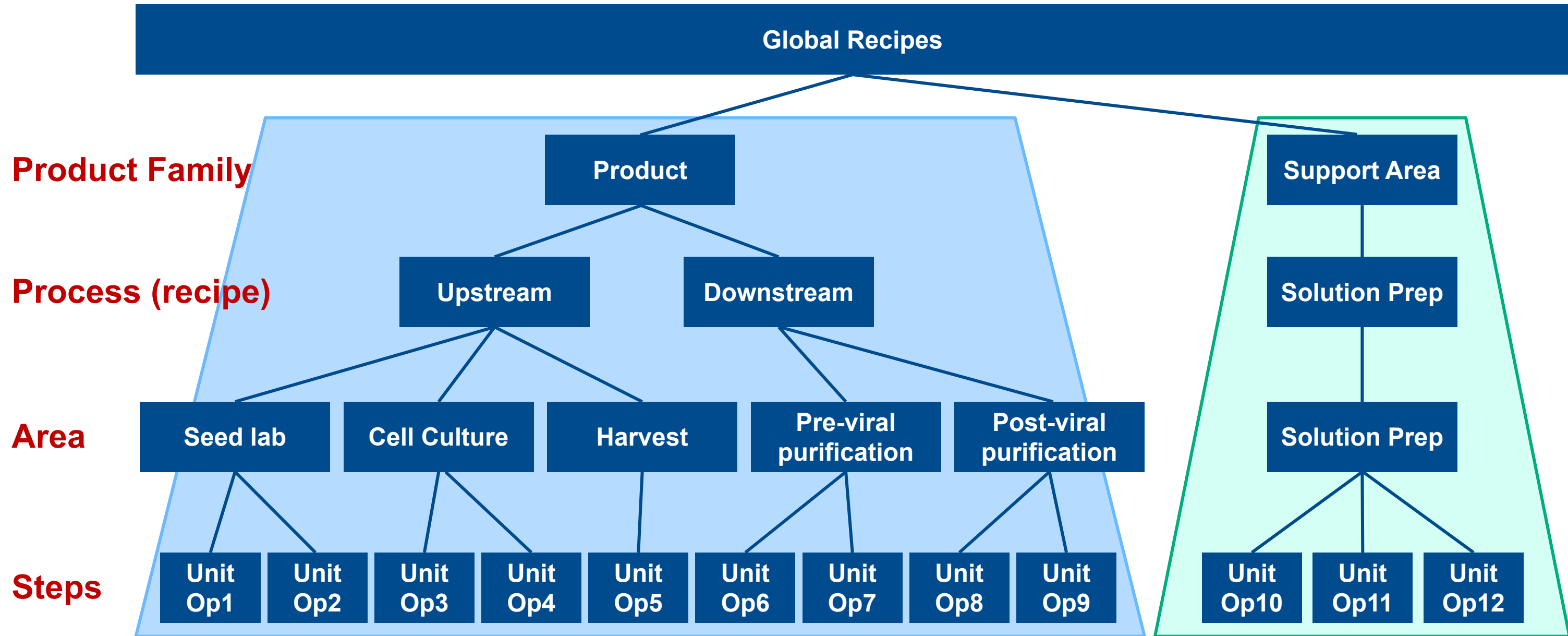
Master Batch Record

subclass	vs	p1 Description	p2 Target	p3 Min	p4 Max	p5 UOM
INITIAL_WFI	OPP	Initial WFI Target Weight	80.0	78.4	81.6	%
INITIAL_TEMPERATURE	OPP	Initial Temperature	N/A	N/A	N/A	DegC
AGITATOR_SPEED	OPP	Agitator Speed	200	195	205	RPM
AGITATOR_SPEED	OPP	Agitator Speed	250	245	255	RPM
ENB_TEMP_CONTROL	CONFIG	Enable Temperature Control	Yes	N/A	N/A	N/A
AGTN_REQ	CONFIG	Agitator Required	Yes	N/A	N/A	N/A
MAT_TO_BE_MADE	CONFIG	Material to be Made	Buffer	N/A	N/A	N/A
MAT_ADD_SOP_NAME	CONFIG	SOP to add Material	COM-MP-XXXX	N/A	N/A	N/A
MIX_TIME	OPP	Mix Time	20	N/A	N/A	Minutes
MIX_TIME	OPP	Mix Time	0	N/A	N/A	Minutes
POST_MIX_TEMPERATURE	OPP	Post-Material Mix Temperature	N/A	N/A	N/A	N/A
FINAL_TEMPERATURE	OPP	Final Temperature	20.0	15.0	25.0	DegC
FINAL_TANK_WEIGHT	OPP	Final Tank Weight	100.0	98.0	102.0	%
FINAL_MIX_TIME	OPP	Final Mix Time	5	N/A	N/A	Minutes
SAMPLING_REQUIRED	CONFIG	Sampling Required (Yes/No)	Yes	2	N/A	PH_COND
PH	OPP	Final pH Results	N/A	6.70	7.30	N/A
COND	OPP	Final Conductivity Results	HO	N/A	N/A	mS/cm
OSMO	OPP	Osmolality	N/A	N/A	N/A	N/A

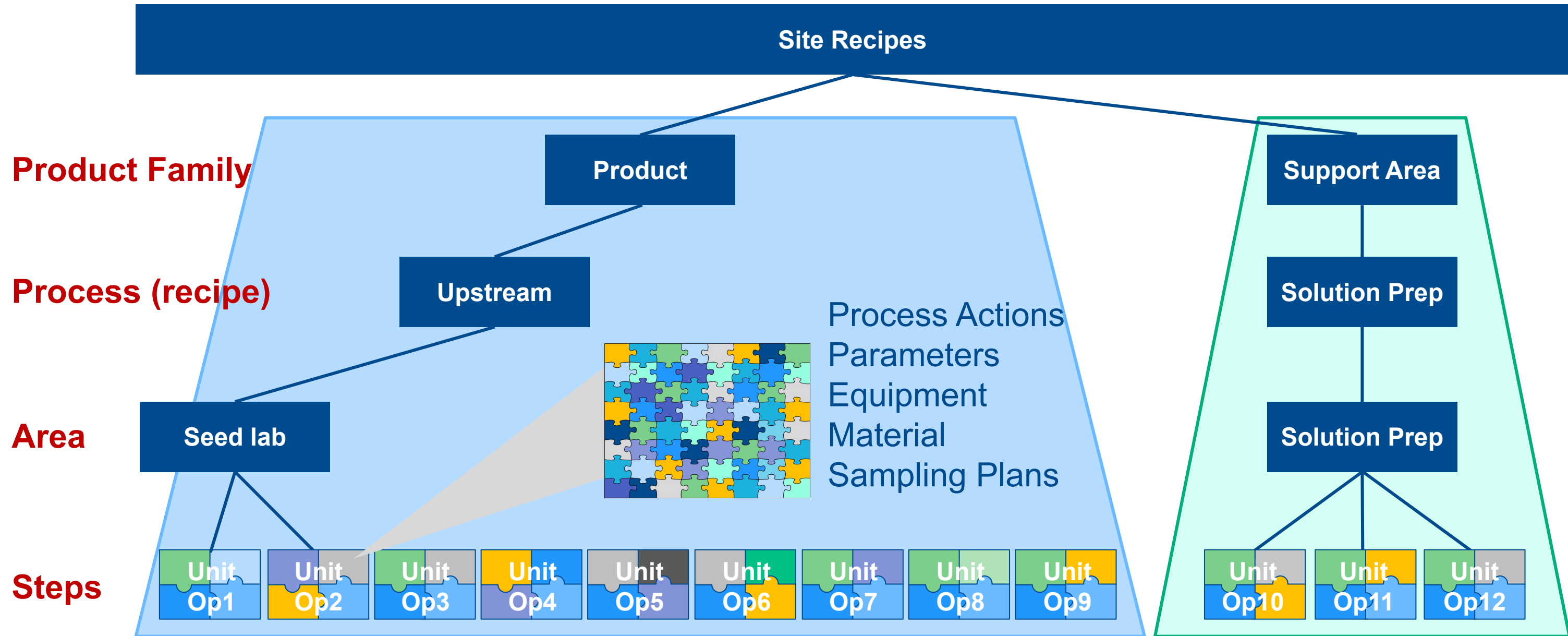
MES Recipe Parameters



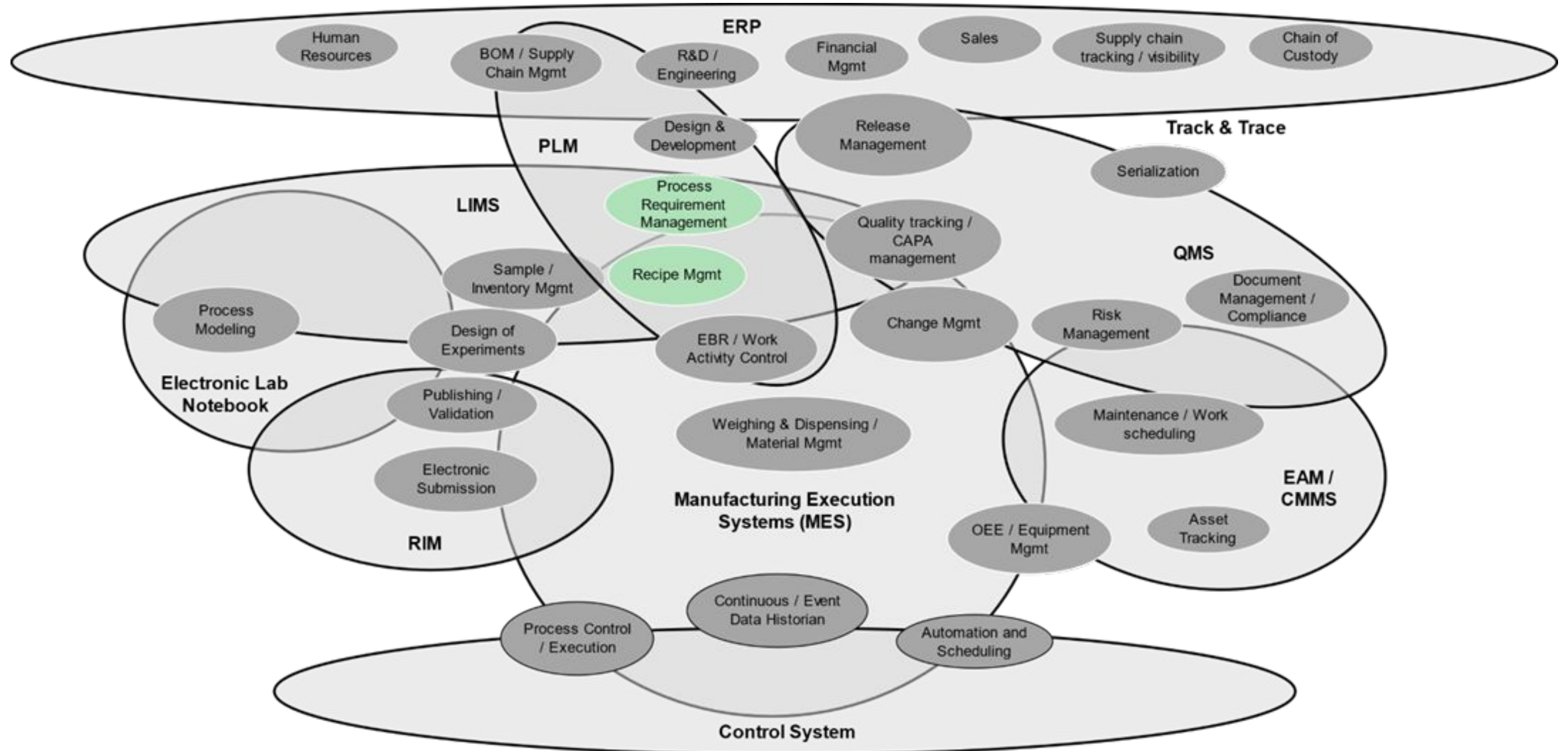
Recipe Modularization



Recipe Modularization



The Knowledge Management Challenge



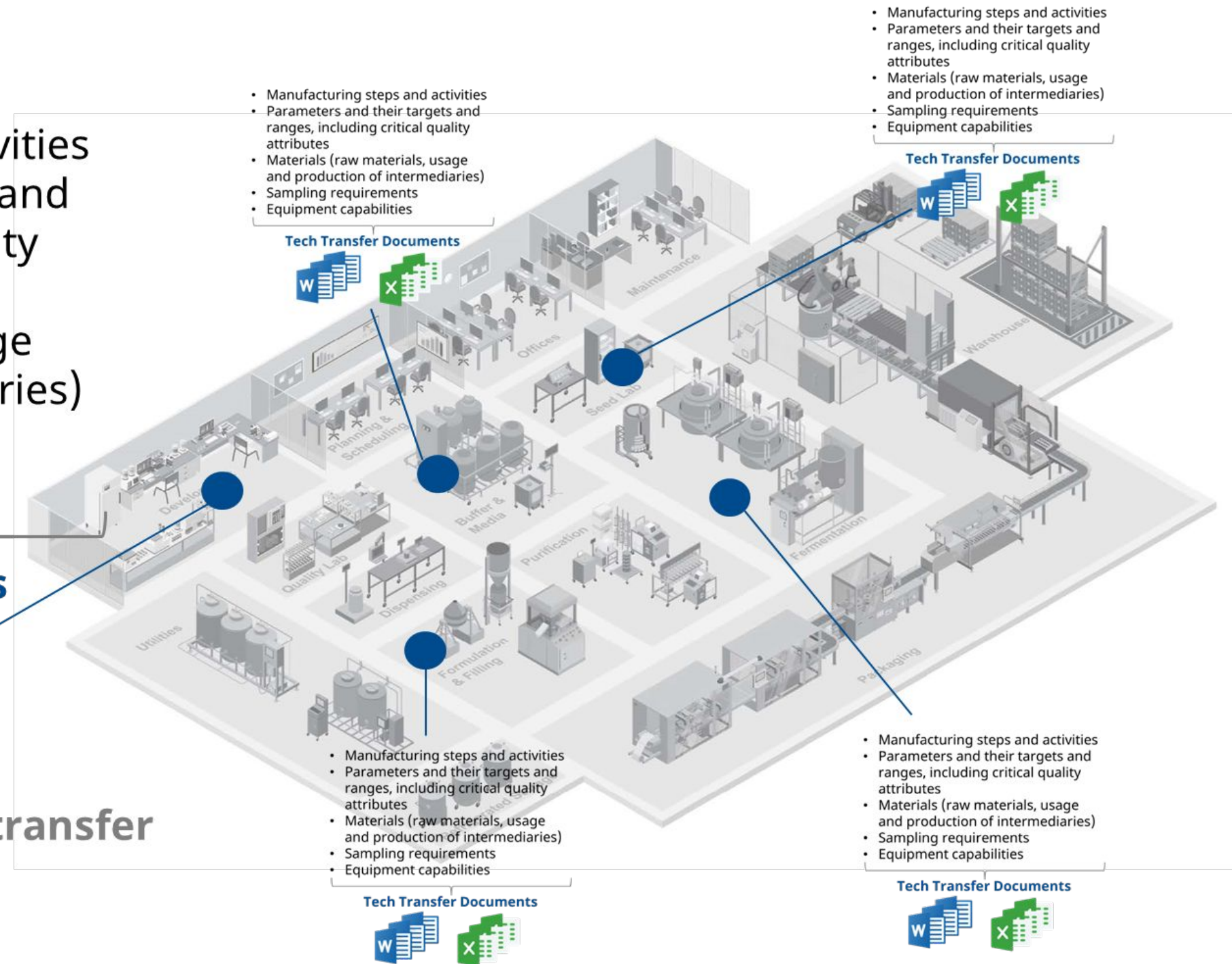
Managing 7000 Parameters per Tech Transfer

- Manufacturing steps and activities
- Parameters and their targets and ranges, including critical quality attributes
- Materials (raw materials, usage and production of intermediaries)
- Sampling requirements
- Equipment capabilities

Tech Transfer Documents

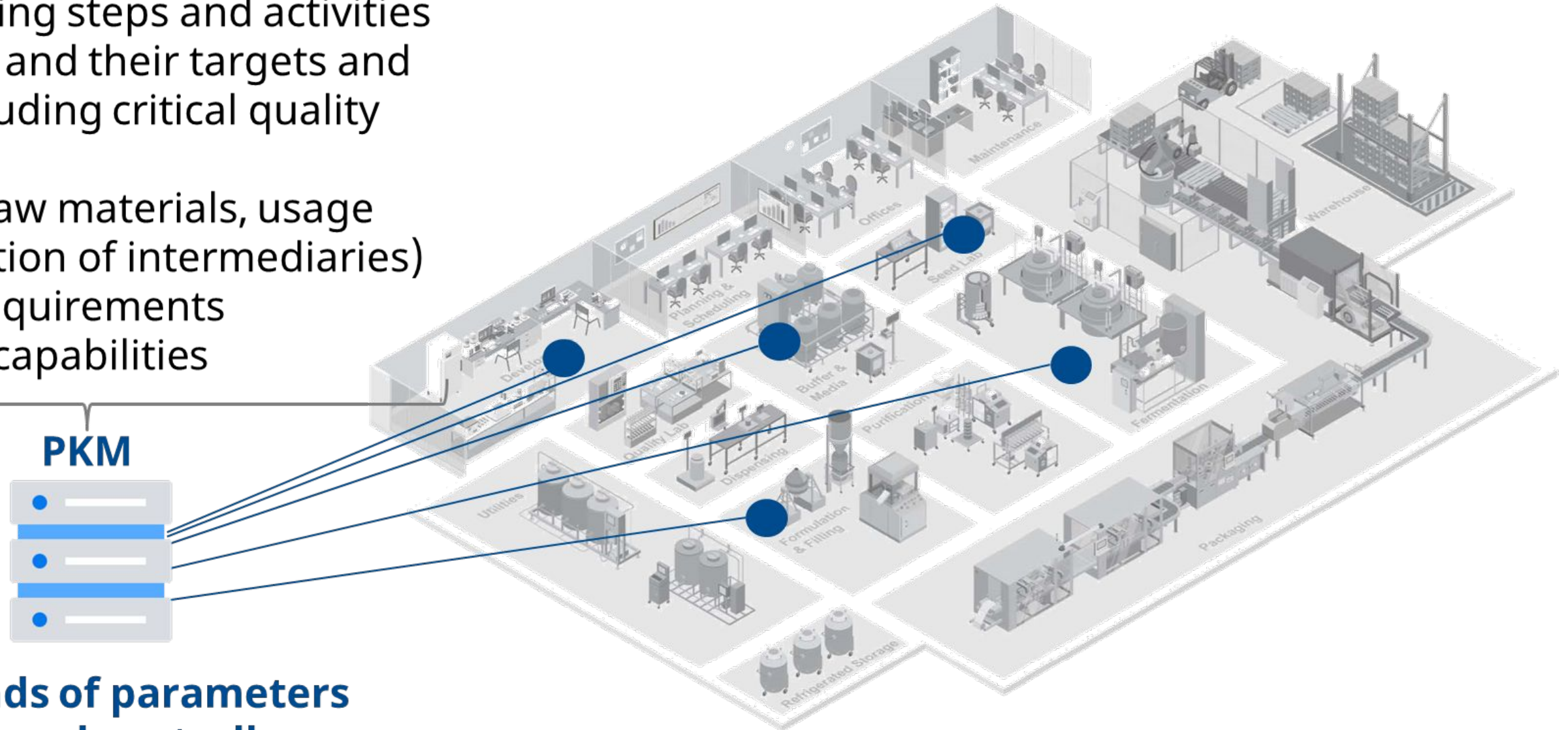


Thousands of hours for manual transfer
Prone to Errors



Digital Recipe Parameter Lifecycle Management

- Manufacturing steps and activities
- Parameters and their targets and ranges, including critical quality attributes
- Materials (raw materials, usage and production of intermediaries)
- Sampling requirements
- Equipment capabilities



**Thousands of parameters
managed centrally**

Example of Mapping Customer Specification to PKM Master Data

No	equipment	operation	Material ID			Material properties				Set Point				Q_Range (NOR)					Q_Range (PAR)							
			material ERP	material ID	material name	state	assay wt%	MW [g/mol]	Dens [kg/m ³]	rel to ref value	rel to ref units	mass [kg]	vol [L]	moles [kmol]	min	max	rel to ref value	rel to ref units	mass [kg]	vol [L]	moles [kmol]	rel to ref value	rel to ref units	mass [kg]	vol [L]	moles [kmol]
1	EQ1	Charge	1001	101	Material 1	solid	100	600		1	kg/kg	180		0.30	min	0.98	kg/kg	176.4								
2	EQ1	Charge (E: 0.93 kg/min) and	1002	102	Material 2	liquid	20	150	1.4	1.1	equ	248	177	0.33	min	1.045	equ	235	168	0.31	1.0013	equ	225	161	0.30	
3	EQ1	Charge (E: 0.98 kg/min) simultaneously	1003	103	Material 3	liquid	20	40	1.3	2.5	equ	150	115	0.75	min	2.375	equ	143	110	0.71	2.2713	equ	136	105	0.68	
4	EQ1	over								5	hours				min	5	hours				-25	hours				
5	EQ1	while keeping the temperature at								-20	°C				min	-25	°C				-25	°C				
6	EQ1	Agitation speed								400	RPM				max	-10	°C				0	°C				

1 [Bioreactor.Charge Material.Material.aq. Edt (15%).Moles Set Point]*[Bioreactor.Charge Material.Material.aq. Edt (15%).Molecular Weight]/([Bioreactor.Charge Material.Material.aq. Edt (15%).Assay]/100)

Calculations in PKM

- Change Management
- Approval Workflows
- Report Generation
- Version Control

Agitation Speed (rpm)
 Charge Temperature (°C)
 Charge Duration (over) (hours)

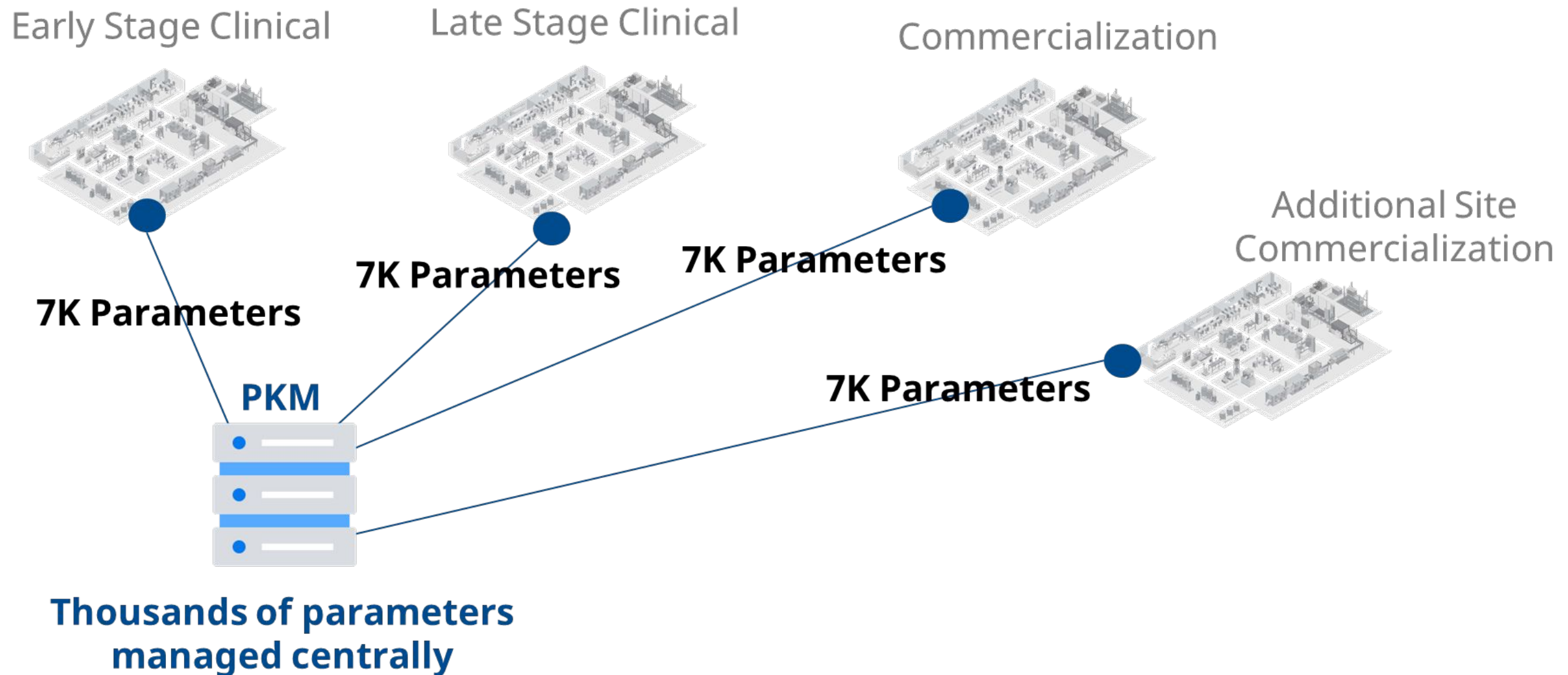
Set Point: N/A 400

Set Point: N/A -20 NOR Min: N/A -25 NOR Max: N/A -10 PAR Min: N/A -25 PAR Max: N/A 0

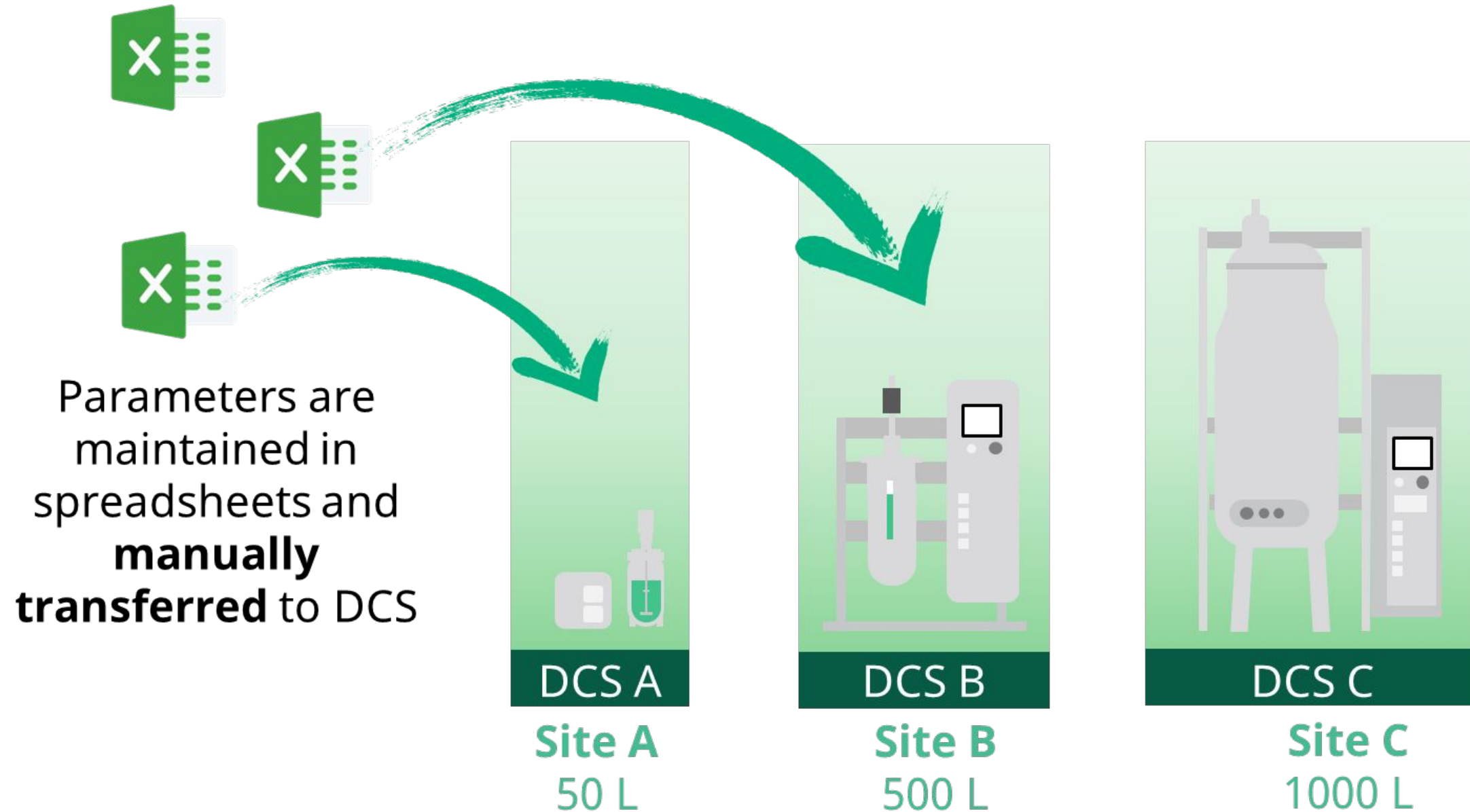
Set Point: N/A 5 NOR Min: N/A 5 PAR Min: N/A -25

Parameters in PKM

Scalable across the Entire Product Lifecycle – 28 K Parameters



Traditional Management of Manufacturing Parameters

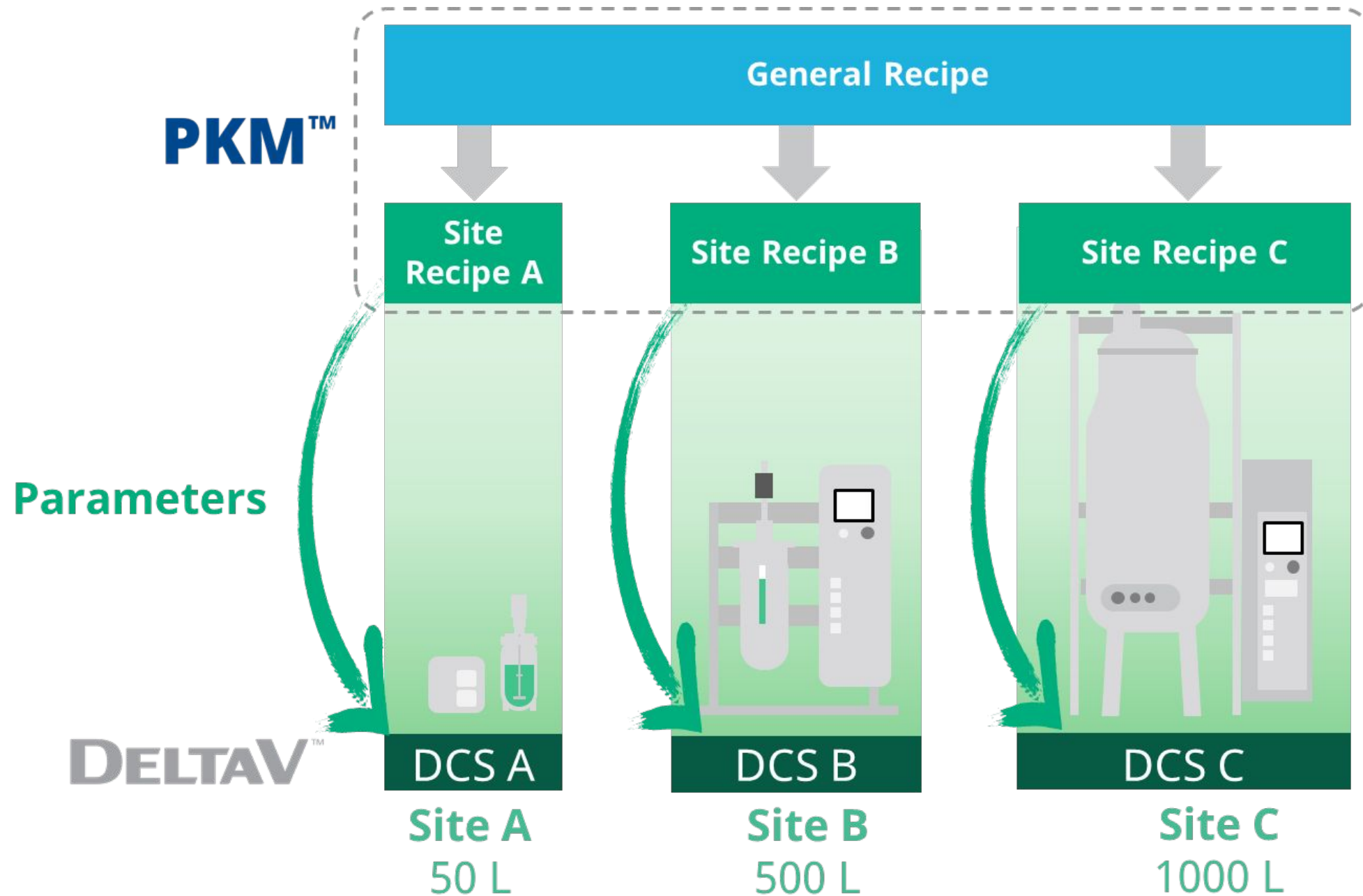


Slow

Prone to errors

Poor change control

Digital Management of Manufacturing Parameters



Fast
Minimal manual tasks
Improved change control

Genentech CSC Facility



SSF CSC SUT Automation Objectives

- **Highly integrated and fully paperless** automation solution
- **Built in flexibility** for clinical (ad-hoc activities) and enabled for launch/commercial
- Introduction to **new technologies** as simplified standards for Review By Exception (RBE), Process and Knowledge Management (PKM), Data Visualization, Analytics and Collection (DVAC)
- **Creation of Standard Automation platform to minimize customization and support rapid deployment to future sites**
- Maximizes efficiency with fewer resources to **significantly reduce environmental impact**



<p>100's Basecamp parameters passed per recipe</p>	<p><5 Minutes from Basecamp approval to MES effectivity</p>
<p>180 GMP recipe objects automatically created</p>	<p>>3 Months saved per tech transfer</p>
<p>0 Hours spent authoring MES or DCS recipes</p>	<p>6-8 Engineers saved</p>
<p>0 Parameters manually entered MES or DCS</p>	<p>\$1m Cost avoidance annually</p>