Methodology for Converting Batch to Continuous

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Systematic workflow with gate reviews

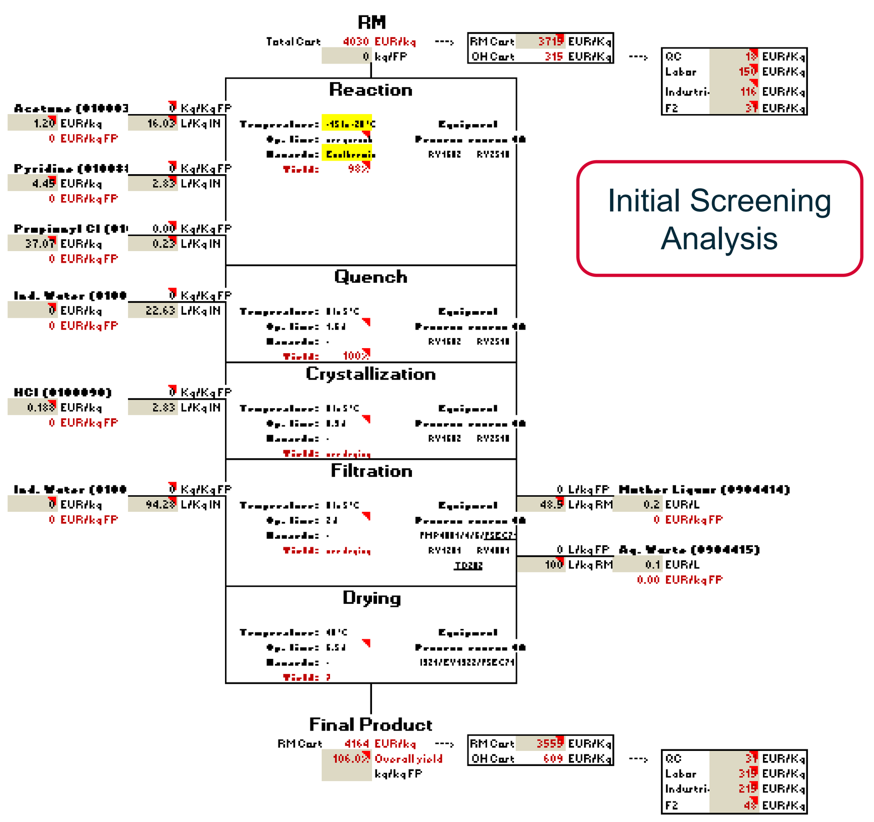
Idea Screening → Technical Evaluation → Development → Scale-up & Engineering → Tech Transfer & Industrialization

Identify Drivers and Objectives

Identify Business Drivers

Safety	Quality	Cost
Efficiency	Time to Market	Environmental Impact

Economic Analysis



Initial Screening Analysis

Science & Technology Assessment

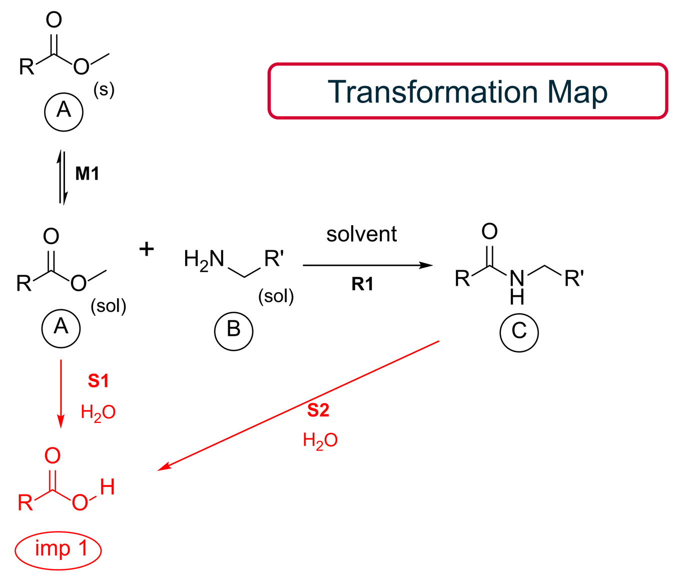
Approaches/Tools

- Adoption of **Quality by Design** lifecycle approach
- Selection of the most appropriate development approach: **DoE** (Modde), **Modeling** (Dynochem, CFD)
- Support activities using **Britest** toolbox and methodologies (ISA, PDD, TM, etc.)

Identify constraints and risks, and develop an understanding of the process

Define Basic Chemistry

Transformation Map



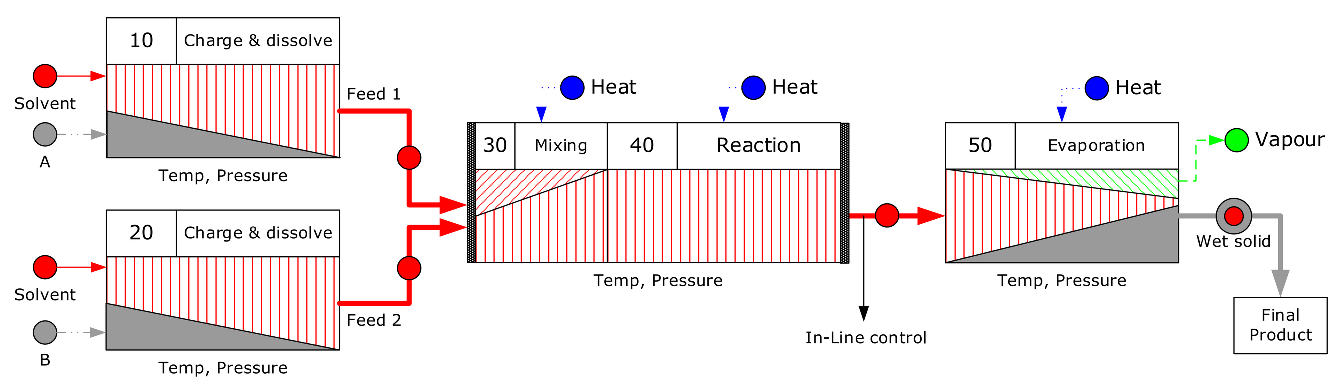
Compatibility Study

	Products				Environment		Materials			
Starting Material	A	B	Solvent	C	Air	Water/ Moisture	Glass	SS	PTFE/ PFA	Gasket material
A		R				D				
B	R									
Solvent										
C						D				

D – Decomposition H – Heat Release R – Main Reaction Im – Immiscible
c – combustion-supporting SR – Side Reaction ? – Information not available

Evaluate Batch Process & Step Continuous Process

Process Definition Diagram



Step	10	20	30	40	50
Notes	No solubility issues	No solubility issues	Exothermic mixture	Reaction has fast kinetics Side product has slow kinetics	

Identify Benefits and Barriers of Flow

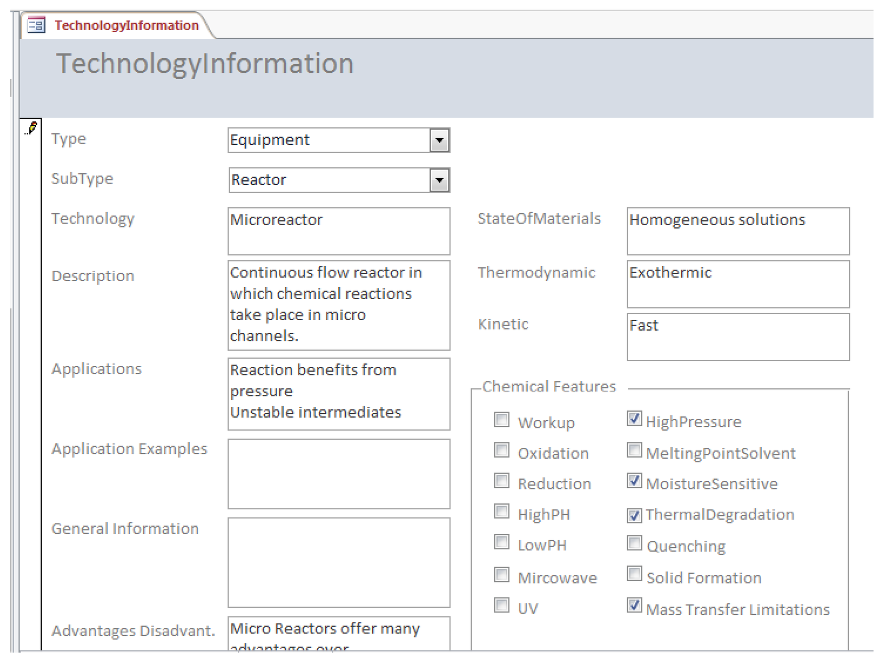
Characteristics	Batch Process		Notes	Benefits						Barriers
	Reaction (Step 1)	Quench (Step 2)		Safety	Cost	Quality	Efficiency	Environmental Impact	Time to Market	
Reaction Rate	15 min (-5-0°C)	10 min (-5-0°C)	Can be improved exploring T or P (intensification)		x	x	x			
Heat Generation	Exothermic addition	Exothermic addition	Cooling system may be required (better T control)			x				
Mass Transfer Limited (reaction or workup)	No	No	Start material cooling or underpressure							
Side Reaction(s)	Yes (significant?)	No	In-line control		x	x	x			
Hazards	No	No	Safer in continuous	x				x		
Work-up	NA	No								

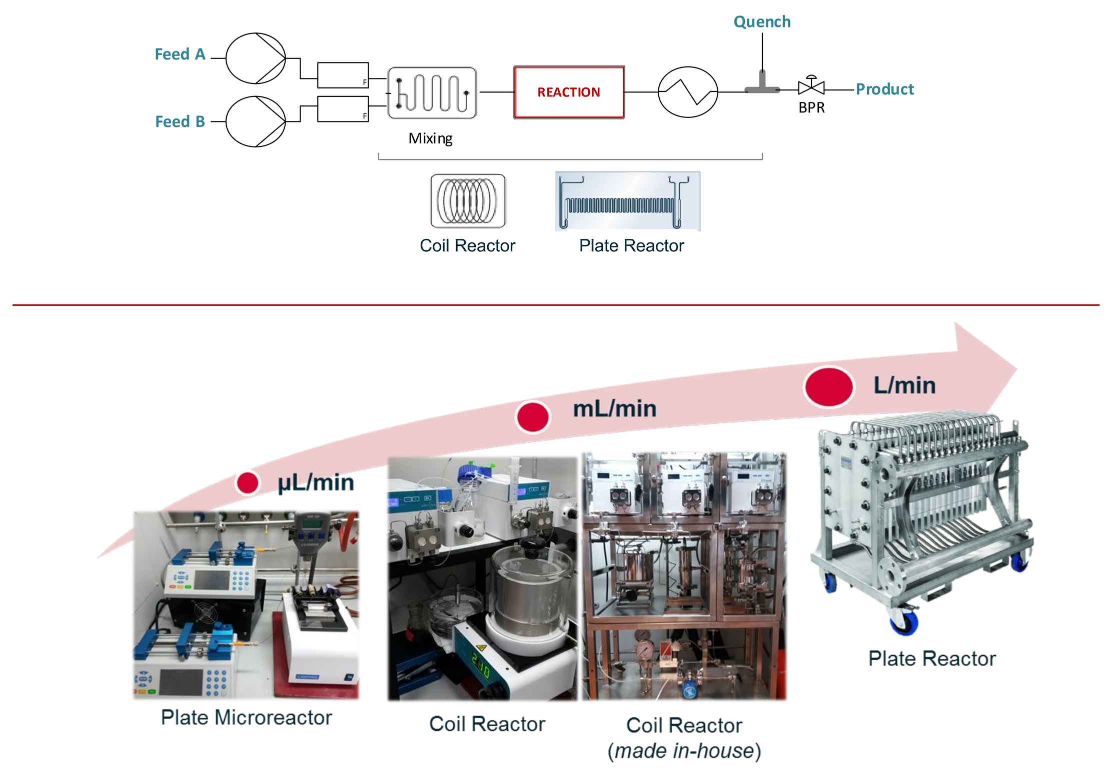
NS – Not Significant T – Temperature t – time P – Pressure NA – Not Applicable
b.p. – boiling point RC – Regulated Compound

Define scale-up approach
Risk Assessment II (FMEA)
Define PAT and Control Strategy
Identify regulatory and compliance requirements

Define Adequate Experimental Setup

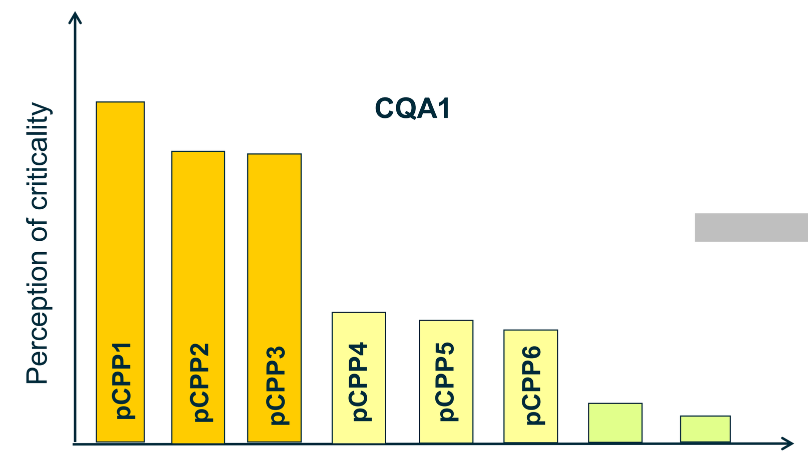
Technology & Applications Database





Risk Assessment I

Potentially Critical Process Parameters (pCPP's)				
Description	Critically perception (1-5)			
	User 1	**User 2**	**User 3**	**Average**
Overall flow rate	5	5	5	5
Ratio A:B	5	5	5	5
Temperature feed A	1	2	1	1
Temperature feed B	1	2	1	1
Reaction temperature	5	5	5	5
Pressure	3	1	2	3

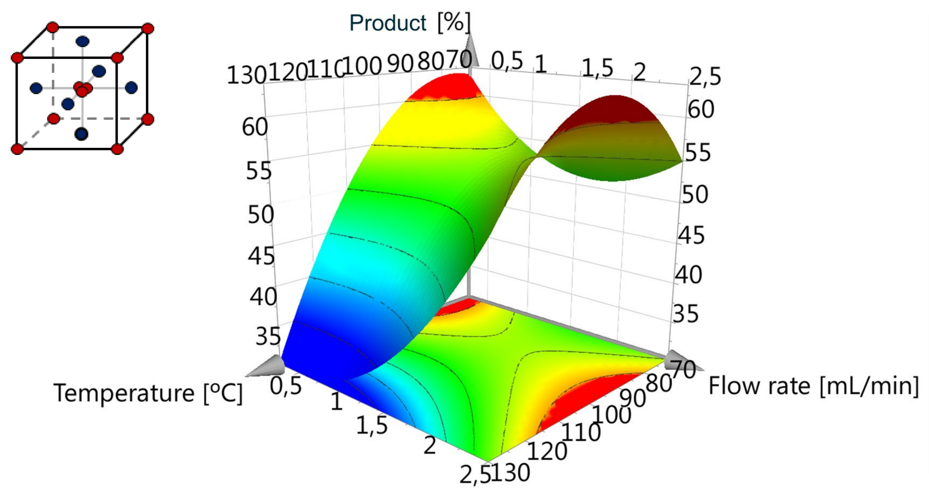


Pareto rule
for many events, ~**80%** of the effects come from ~**20%** of the causes

Prove of Concept, Process Understanding, and Optimization Studies

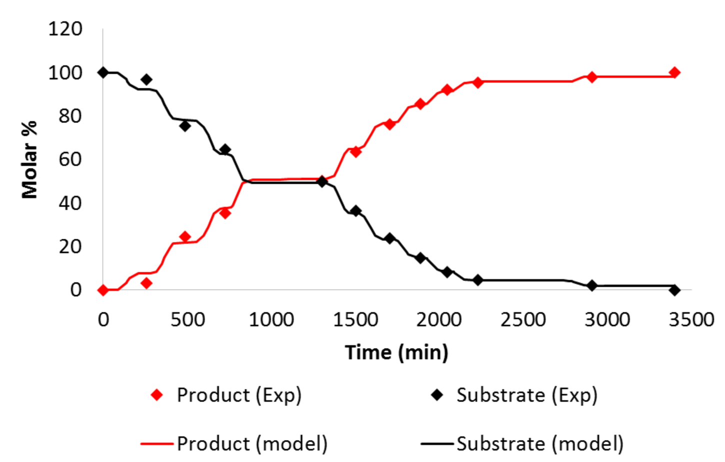
Design of Experiments (DoE)

- Optimization of process parameters
- Evaluate interactions between process parameters



Kinetic Modeling & Simulation

- Determine operation kinetics
- Predict operation scale-up



Computational Fluid Dynamics (CFD)

- Evaluate flow regime
- Evaluate impact when scaling-up