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Process Safety – Chemical Engineering Collaboration to Support Early Phase Acceleration

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Background

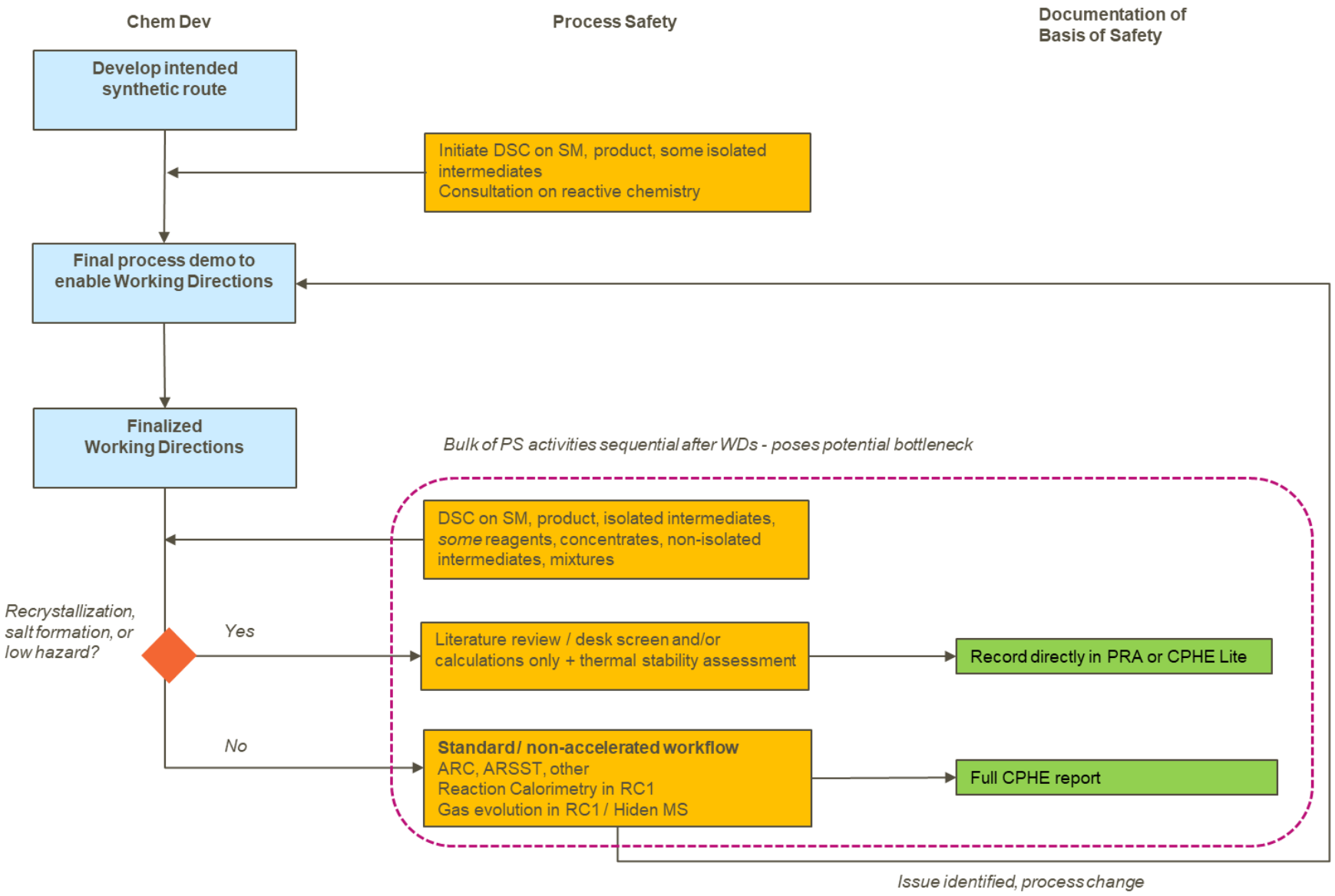
Drivers

- Corporate: Ambitious for Patients to Deliver What Matters Better and Faster
- Division: Accelerate Early Phase Critical Path Activity
- Pilot Plant Department Workshop (2019)
  - Identify critical path activities
  - Define & Drive simplification projects to enable pipeline acceleration
- Internal early phase workload increasing
- Maintain current standards for Basis of Safety

Process Safety Hazard Evaluation - Key Activity with Potential to Accelerate

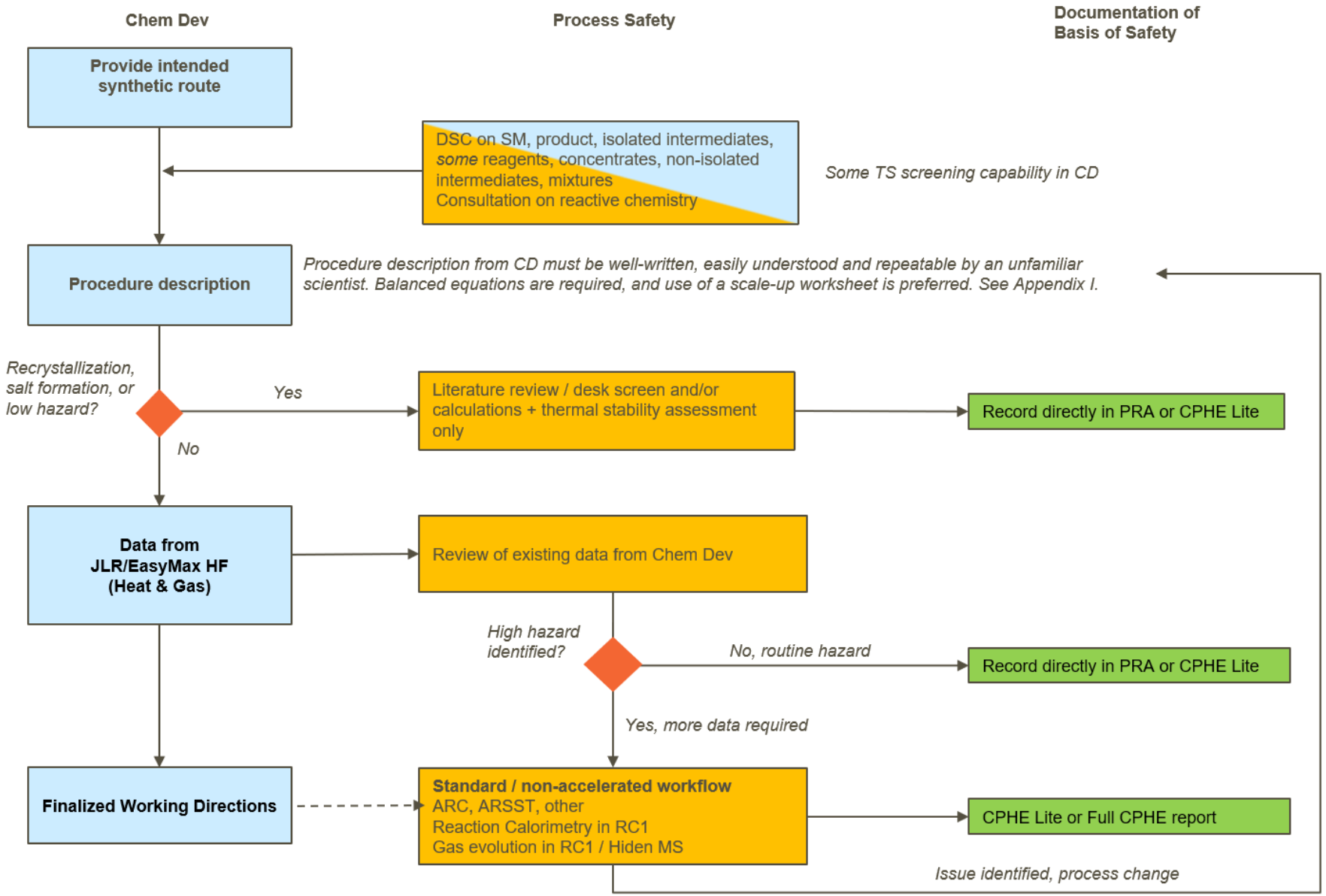
Legacy Hazard Evaluation Workflow for Early Phase

Sequential



Accelerated Hazard Evaluation Workflow for Early Phase

Concurrent



JLR = Jacketed Laboratory Reactor

Accelerated Hazard Evaluation Reporting Matrix

Fit For Purpose

Scale

Hazard

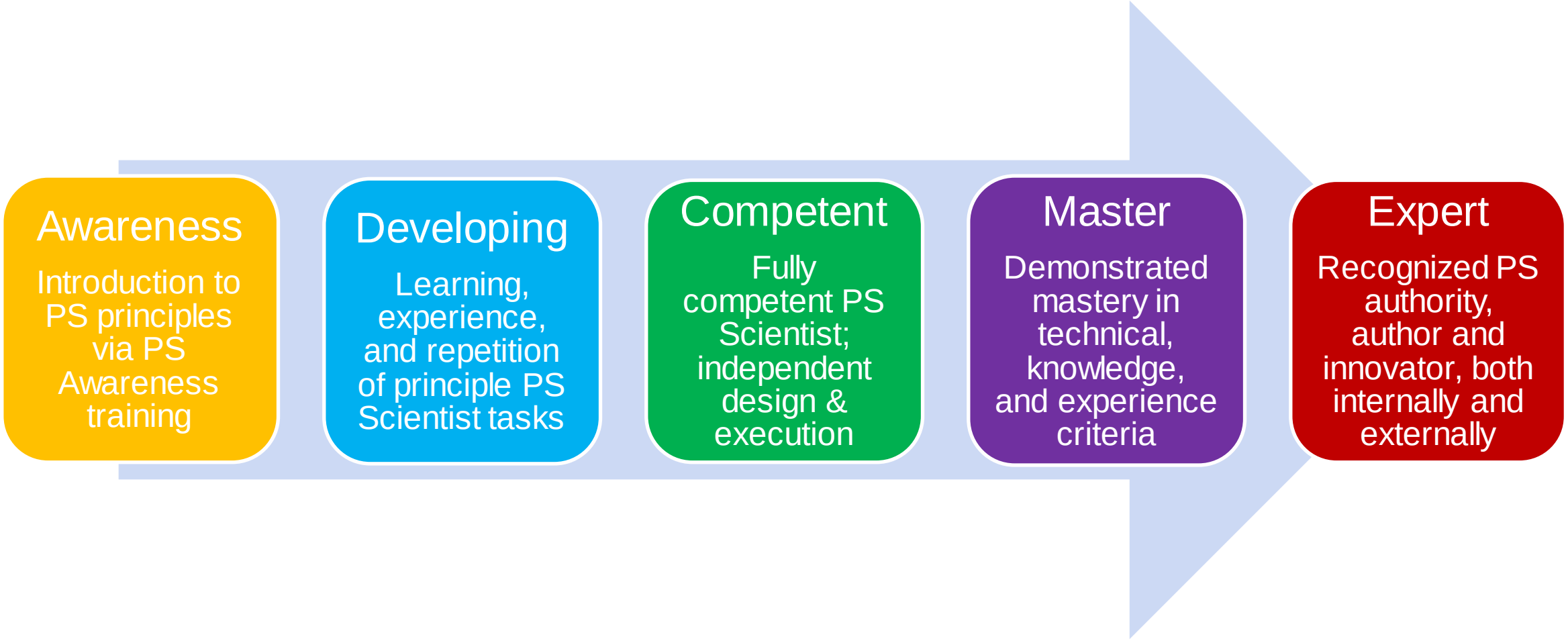
Reporting of safety assessment. Minimum standard

	20L JLRs	Early Phase PP	Late Phase PP Tech Transfer/Lifecycle
Recrystallisation			
Salt formation			
Low hazard chemistry			
Routine hazard chemistry			
High hazard chemistry			

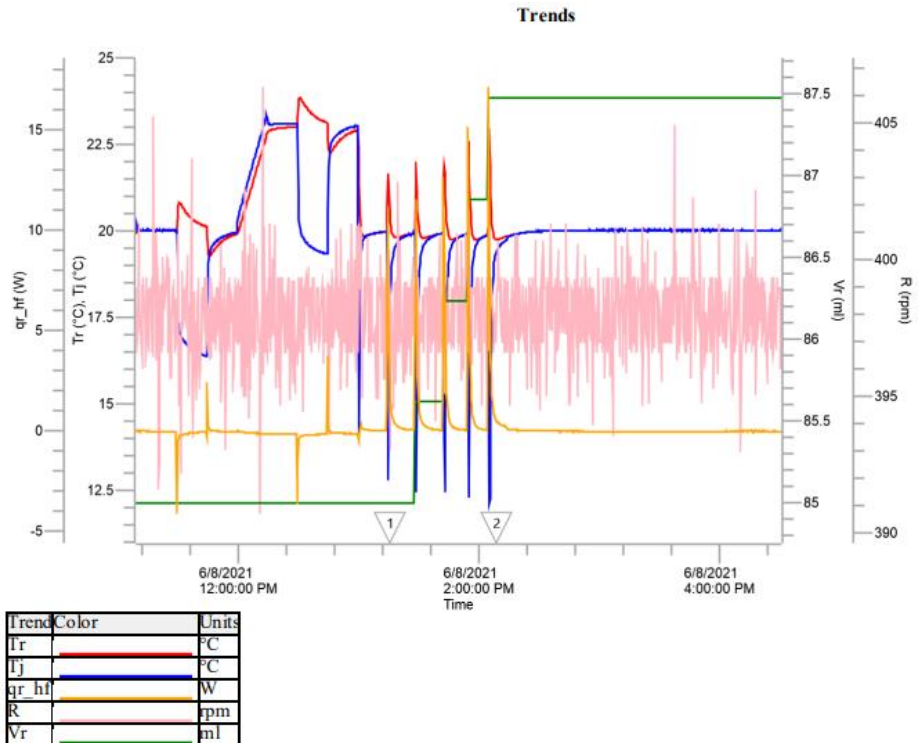
Full Report
Lite Report
PRA direct, no report

Process Safety Scientist Competency Matrix

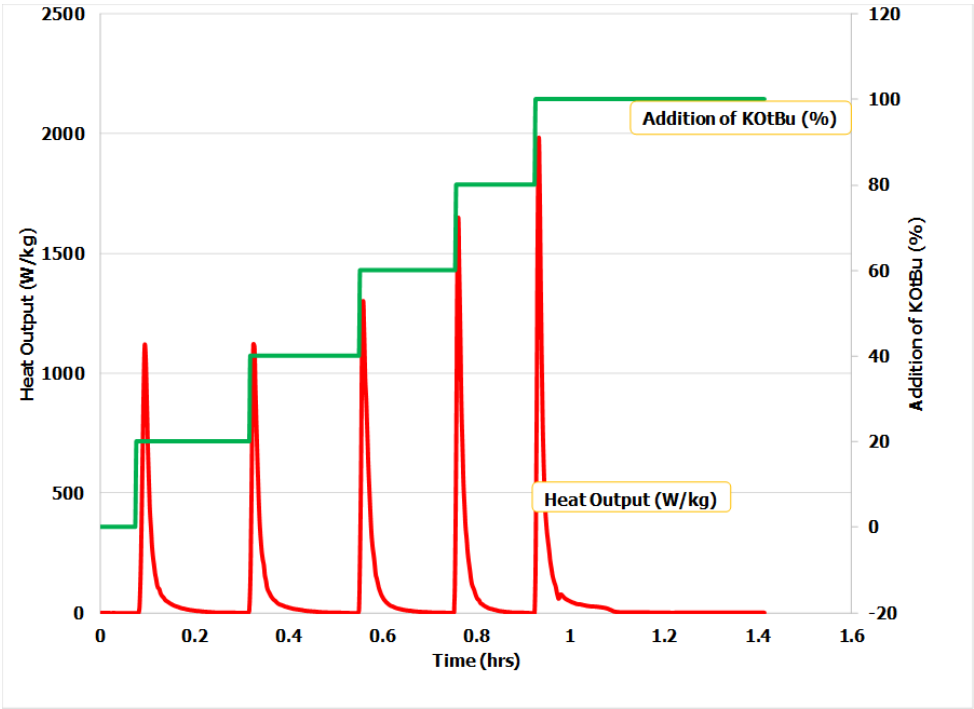
Progression via detailed criteria

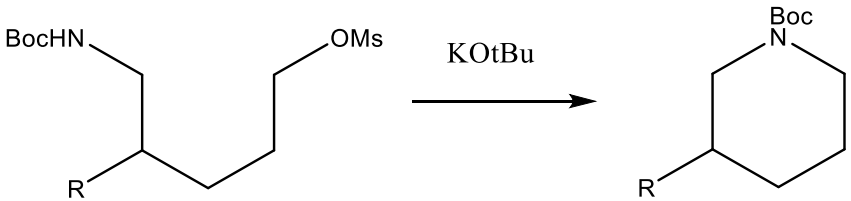


Example – Routine Hazard Process BoS via 100 mL EasyMax Development Run



- Total heat output = **196 kJ/mol (exo)**
- Avg rate heat output = **1279 W/kg**
- PAT R = **35 °C**

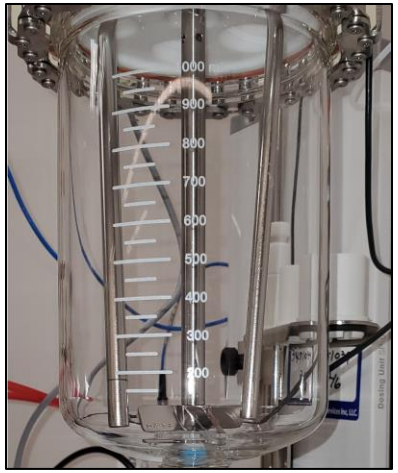




*Execution and data provided by Grace Price

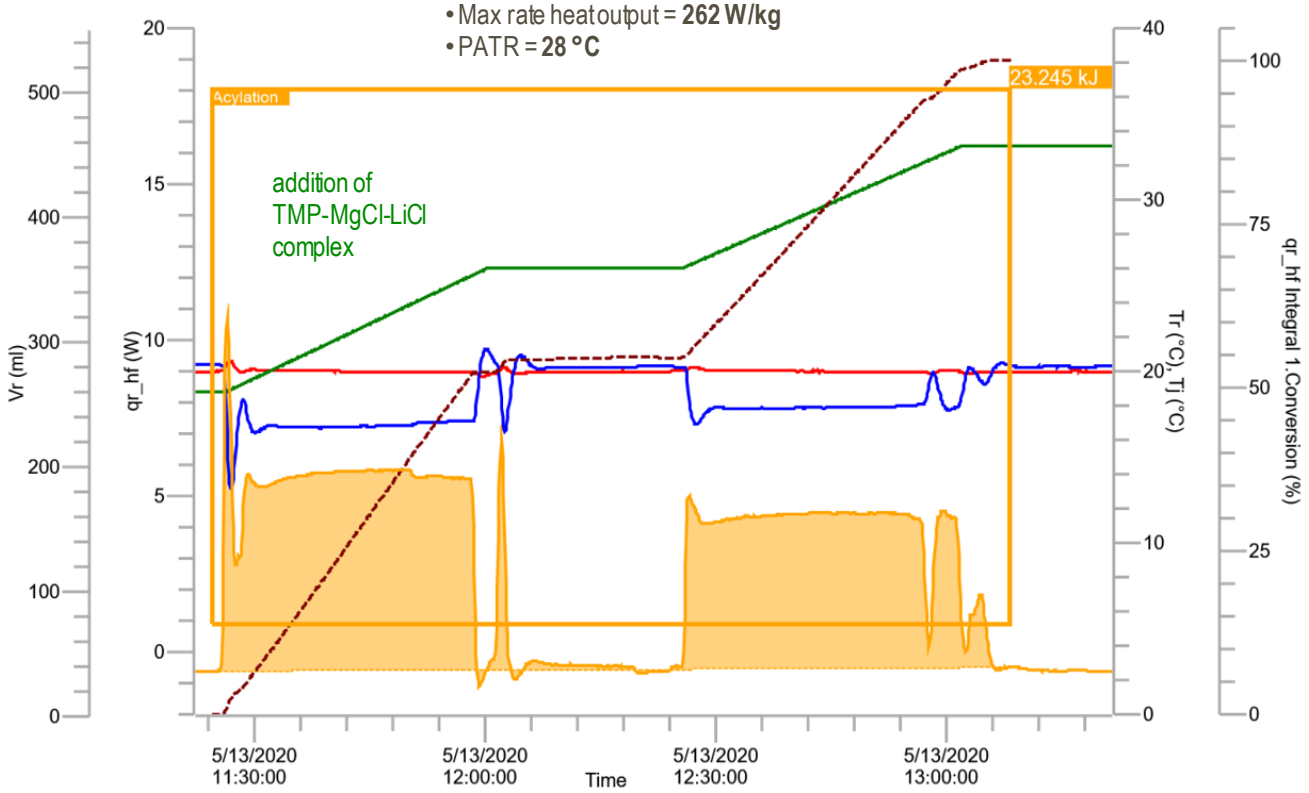
10 g development run, 100-mL EasyMax

Example – Hazardous Process BoS via 1L OptiMax Development Run



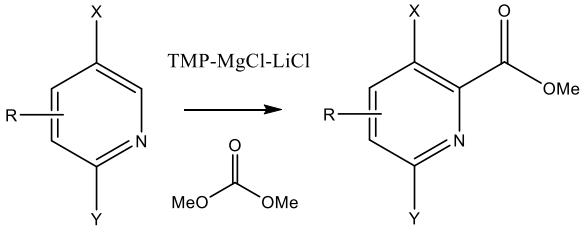
Mettler HFCal	Easymax	Optimax
Vessel size	100 mL	1 L
Minimum fill for HFCal (mL)	~35	~200
Maximum fill for HFCal (mL)	120	1000
Calibration heating element	5 W	10 W
UA (W/m²K) U (W/K)	67 – 175 0.59 – 1.17	79 – 102 1.64 – 3.34

- Total heat output = **152 kJ/mol (exo)**
- Max rate heat output = **262 W/kg**
- PATR = **28 °C**



Trend	Color	Units
Tr		°C
Tj		°C
Vr		ml
qr_hf		W
qr_hf Integral 1.Conversion		%

43 g development run,
1-L OptiMax



*Execution and data provided by Eric Ricci

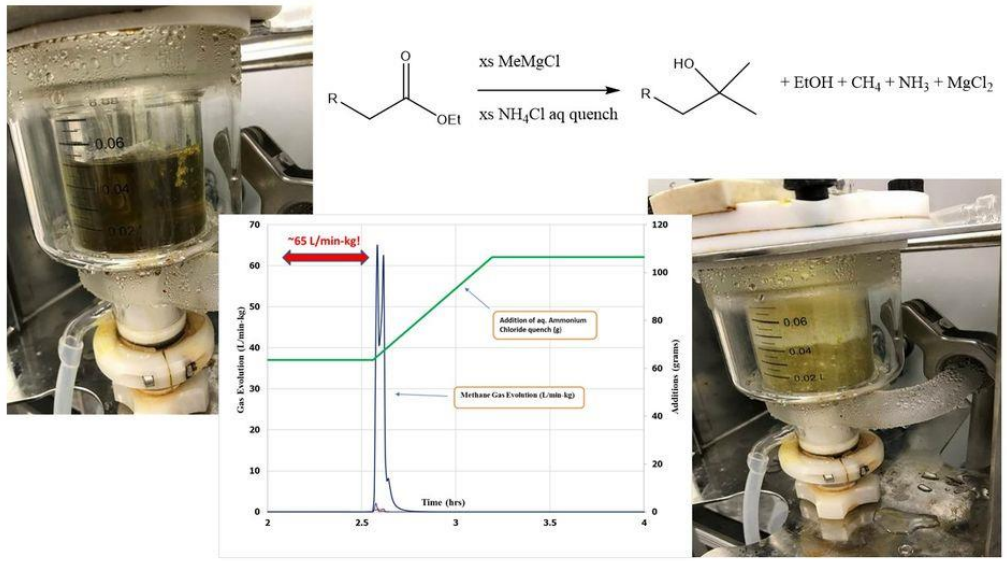
Example – High Hazard Process BoS via RC1 + JLR Data Collection

Copious off-gassing and exotherm observed in early 80 mL RC1 run. Significant hazard identified.

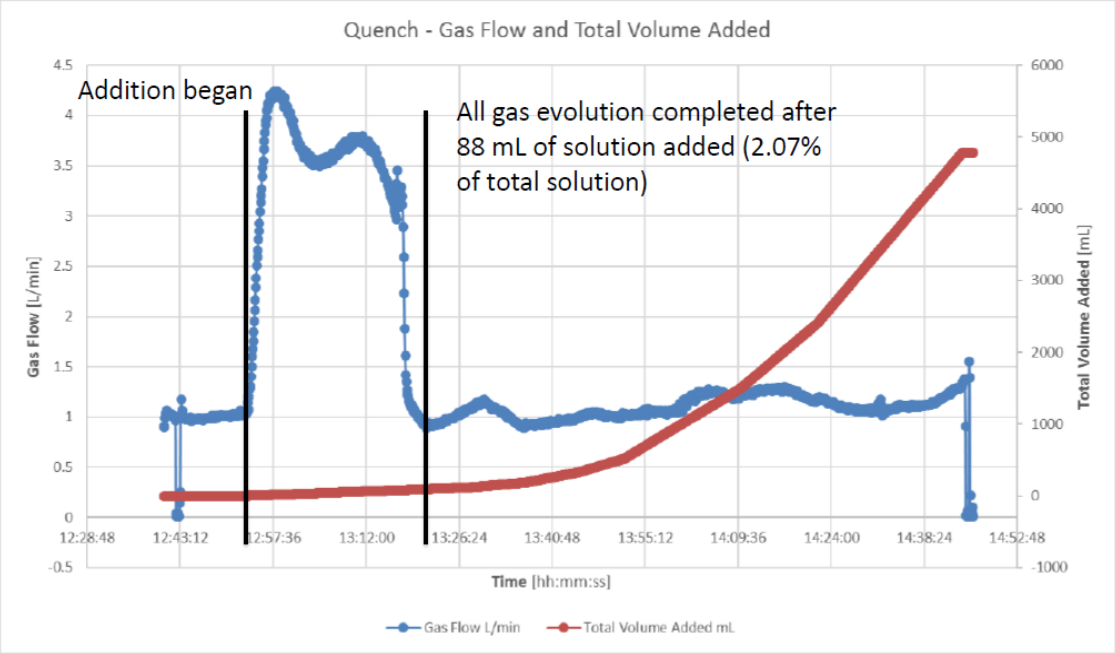
Collaboration between engineering, chemistry, Process Safety, and Pilot Plant.

- Implemented off-gas measurement on 6-L & 16-L scale-up batches. Generated data + process knowledge. Basis of safety was established (i.e., addition rate control).
- No additional safety testing required; CD data incorporated in CPHE report

Process safely scaled into Pilot Plant.



*Execution and data provided by Frank Dixon



*Execution and data provided by Megan Ketchum

Accelerated Workflow Implementation

Benefits & Value Realized

Benefits

- Faster delivery of hazard evaluations, maintaining safety standards
- Earlier hazard evaluation identifies potential showstoppers sooner; less repeat work
- Potential for advanced process understanding (development) using calorimetry data
- Increased process safety awareness and competency within Chem. Eng. Dept.
- Reduced hazard evaluation documentation for lower risk processes

1H2020 for Plant Facing Campaigns

- ~45% Increase in speed (for hazard evaluations) to Pilot Plant
- ~12 Weeks saved on material (not needed) preparation time
- Several hundred grams NCEs not required (costly, short supply)
- ~1.5 FTE savings for process safety support & material preparation
- Safety enhancement: reduced handling for OHC4/5 in laboratory

Acknowledgements

PS – Chem. Eng. Collaboration Champions (partial)

- Nick Falco – Chem. Eng., Project implementation co-lead
- Eric Ricci – Chem. Eng., Collaboration lead
- Frank Dixon – Process Safety, Collaboration lead
- Megan Ketchum – Chem. Eng., JLR Champion
- Grace Price – Chem. Eng., Collaboration partner