Continuous Manufacturing of Drug Substance: Case Studies

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Learning Objectives

1. Cite Unique Challenges for Continuous Manufacturing of Drug Substance.

2. Identify Ways to Systematically Understand Your Process.

3. Develop Ways to Demonstrate Process Robustness.

Continuous Manufacturing

Manufacturing

Unit Operations

Configuration

Controls

PAT

Data Analysis

Continuous Manufacturing of Drug Substance

Chemistry

SMs, Intermediates

Reactions, Work-Up

Manufacturing

Unit Operations

Configuration

Controls

PAT

Data Analysis

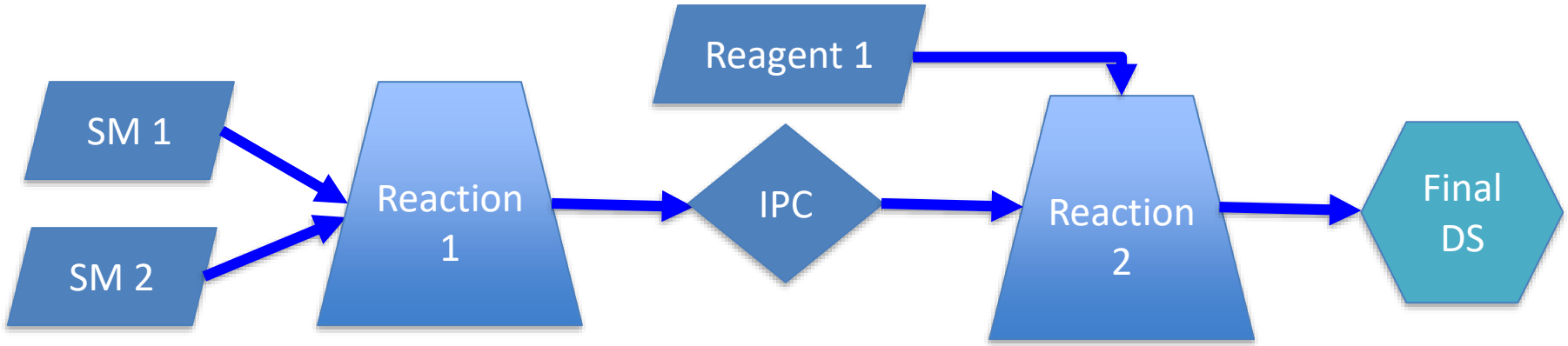
Can You Walk the Process?

Did You Lock the Process?

Walk the Process

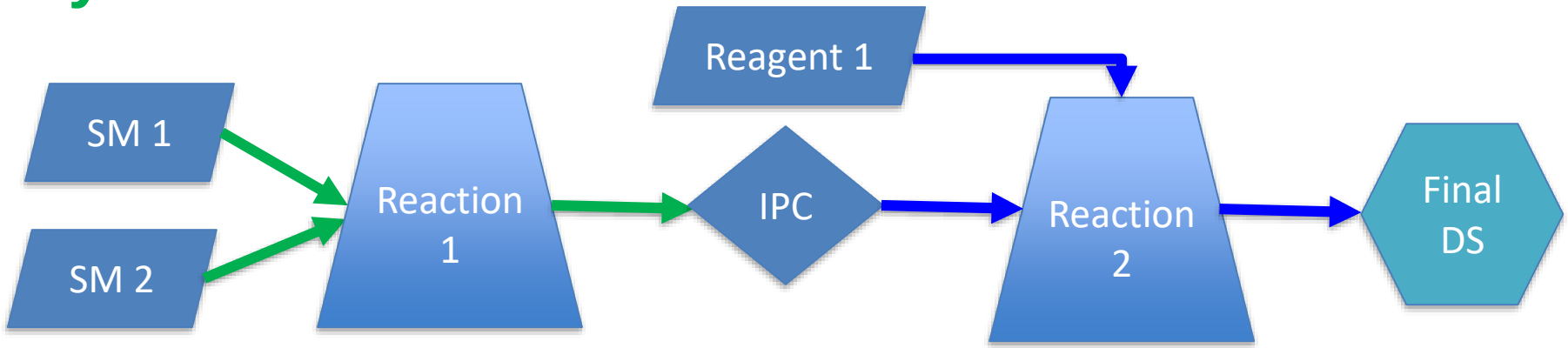
- **Track the Reaction Material**
- **Consider All Routes**
- **Paper Trail**

Case Study

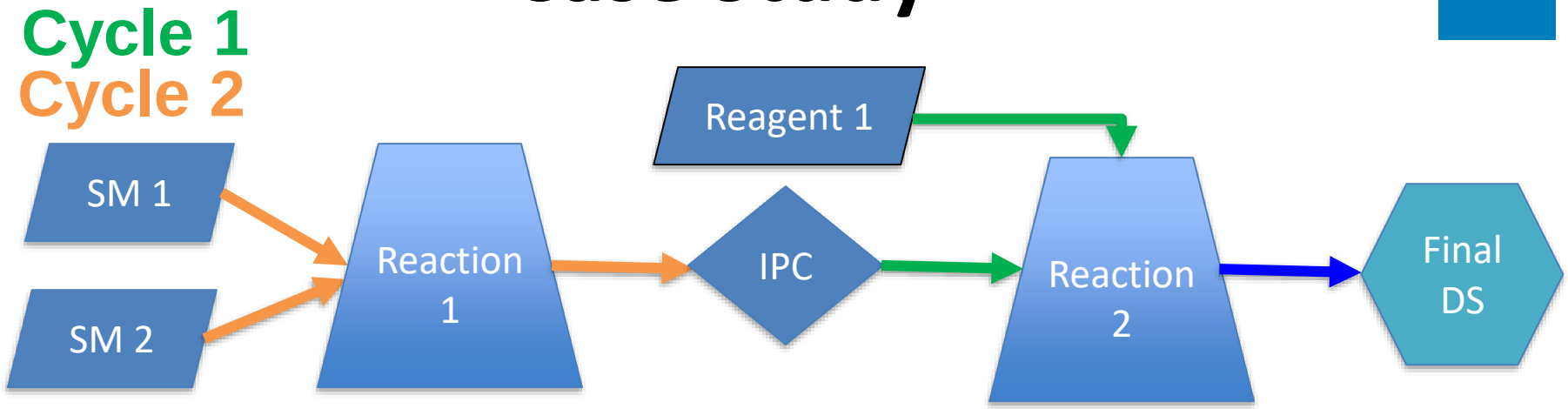


Case Study

Cycle 1

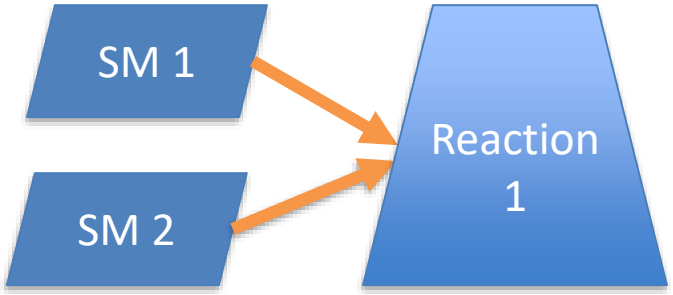


Case Study


Cycle 1
Cycle 2
SM 1
SM 2
Reaction 1
Reagent 1
IPC
Reaction 2
Final DS

Case Study – Reaction 1

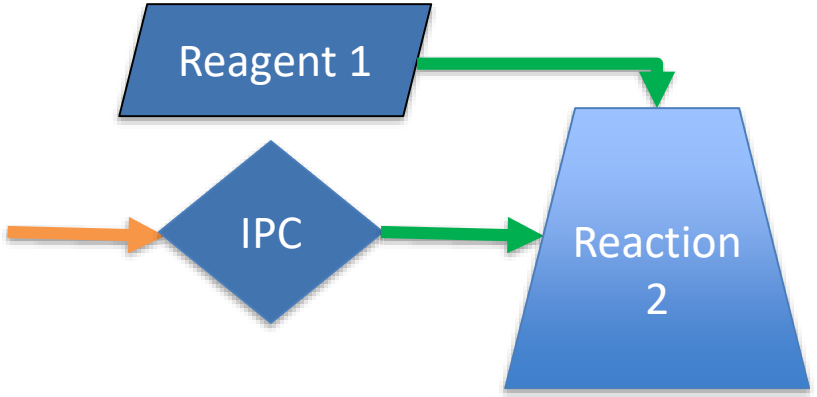
Cycle 2



Track Reaction	Routes	Paper Trail
Reaction Conditions Monitoring CPPs	Start Up of CM	Development Report SOPs

Case Study - IPC

Cycle 1
Cycle 2



Track Reaction

IPC Result Delays

Impact on Cycle 2

Routes

Diverting Material

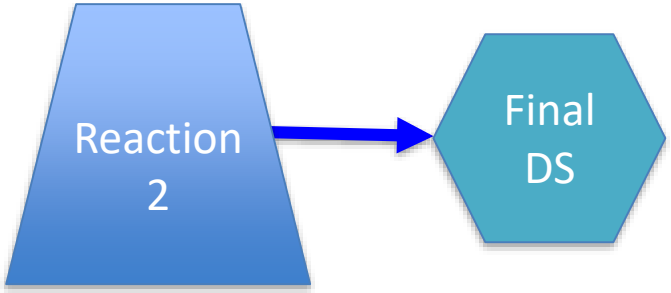
Paper Trail

Schematics

Calculations

Run Charts

Case Study – Reaction 2



Track Reaction

Reaction Conditions

Cycles in DS Batch

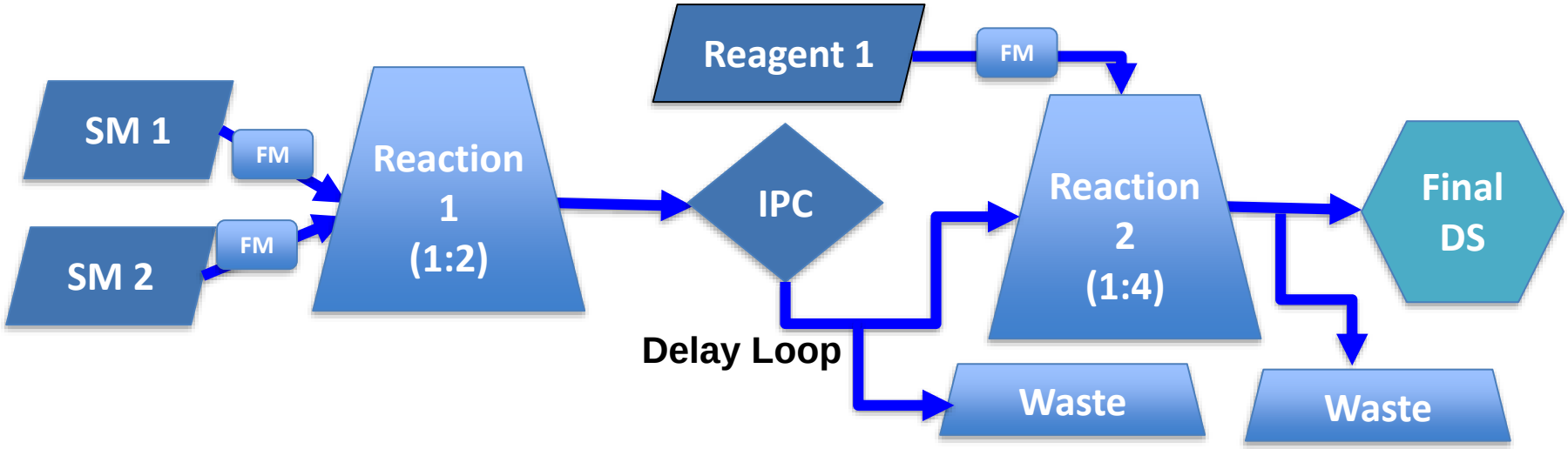
Routes

Shutdown of CM

Paper Trail

Batch Record

How Far We've Come…

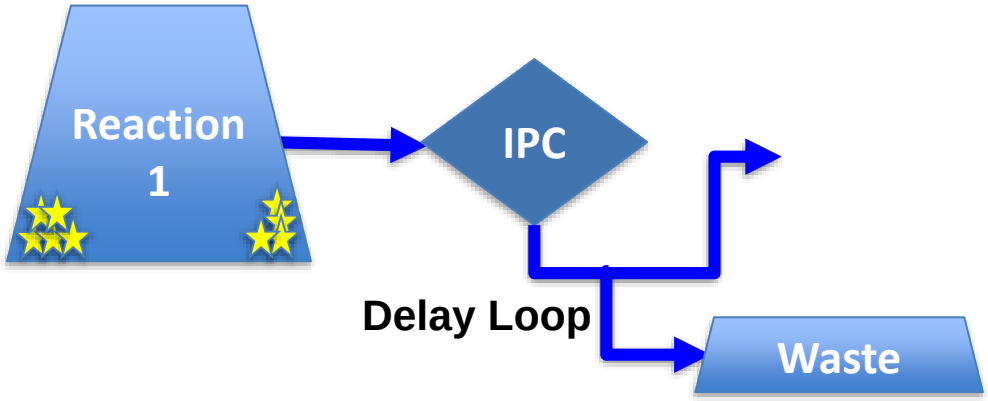


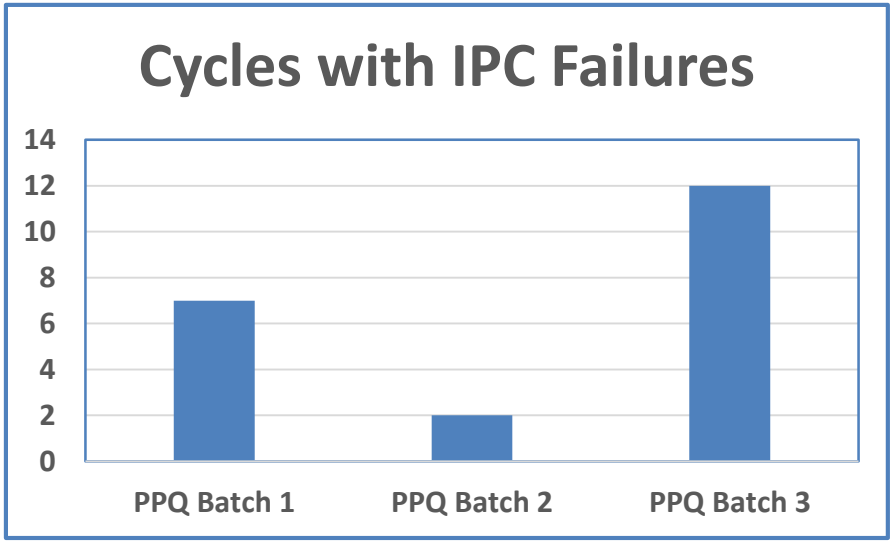
10 Cycles = 1 DS Batch

Lock the Process

- **Confirm Process Robustness**
- **Fully Investigate and Correct Deviations**

Case Study – Build Up





Is the Process Locked?

Case Study – Repeated PPQ

Parameter Tested	Acceptance Criteria	Results
Yield for Continuous Reactor 1 and Reactor 2	To be Established from Commercial Batches	NA
Critical Quality Attributes	Within Established CQA Limits	Conforms
Critical Process Parameters	Within Established CPP Limits	Conforms

Is the Process Locked?

Walk & Lock

Be Transparent

Pre-Operational Visit

Data, Data, Data

Root Cause Analysis

Thoughtful PPQ

Challenge Question #1

True or False

Process development reports, SOPs, and batch records are appropriate mediums to walk through a Drug Substance Continuous Manufacturing process with the ETT or within an application.

Challenge Question #1

True or False

Process development reports, SOPs, and batch records are appropriate mediums to walk through a Drug Substance Continuous Manufacturing process with the ETT or within an application.

True

Challenge Question #2

True or False

When discussing Continuous Manufacturing of Drug Substance with the ETT, your manufacturing process should be locked.

Challenge Question #2

True or False

When discussing Continuous Manufacturing of Drug Substance with the ETT, your manufacturing process should be locked.

False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