
conneqt
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PHARMA

Environmental Monitoring System Investigation

Kevin Louie

Sanofi

About Me

Westchester, NY

Lehigh University
Bethlehem, PA

BS Chemical Engineer,
Class of 2018

Sanofi
Swiftwater, PA

('18 - '20) Rotational Program
('20 - '22) Reliability Engineer
('22 – *) Automation Engineer

sanofi

French multinational Pharma Company headquartered in Paris, France

Immunology, neurology, oncology, rare diseases, diabetes & cardiovascular

Employs over **82,000 people** operating in over **100 countries** serving patients **worldwide**

Site Summary

Swiftwater is a 127-year-old site, in **vaccines manufacturing organization**. It was originally a smallpox vaccine site and later introduced influenza, yellow fever, and meninge vaccines.

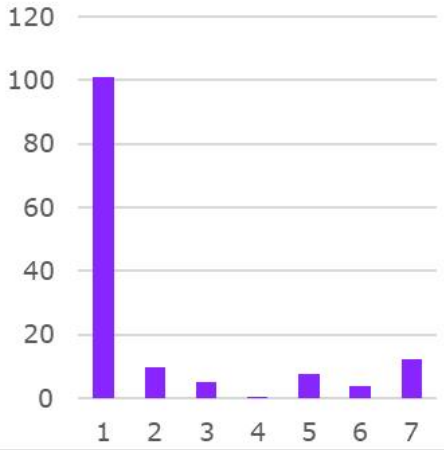
Present at all stage of manufacturing: **seed, antigen, formulation, filling (lyo, vial, syringes), inspection, packaging, and distribution**

63 buildings sitting on 550 acres

Business

- ~142 Mds released 2024
- Licensed in 100 countries
- 3.5Bn€ sales

Flu Products: 101Mds
Menactra: 6.9Mds
MenQuadfi: 7.1 Mds
YF-Vax: >1 Mds
Adacel: 10 Mds
Pentacel: 4 Mds
Other: 12 Mds



Main Products

Swiftwater Site Produced

Influenza Vaccine Fluzone®
YF-VAX® Yellow Fever Vaccine
MenQuadfi Meningococcal (Groups A, C, Y, W) Polysaccharide Tetanus Toxoid Conjugate Vaccine (MenACYW conjugate vaccine)
Influenza Vaccine Fluzone® High-Dose
Efluelda INFLUENZA VACCINE
Menactra Meningococcal (Groups A,C,Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine

Pearl River Produced

Influenza Vaccine Flublok®
Supemtek Quadrivalent Recombinant Influenza Vaccine

Multi-Site Produced

vaxelis
DAPTACEL Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed
Adacel Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed
TENIVAC™ Tetanus and Diphtheria Toxoids Adsorbed
ActHIB Haemophilus b Conjugate Vaccine (Tetanus Toxoid Conjugate)
Pentacel® Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Inactivated Poliovirus and Haemophilus b Conjugate (Tetanus Toxoid Conjugate) Vaccine
Praluent® (alirocumab) Injection
Beyfortus™ (nirsevimab-alip)

Overview

Seeq x Sanofi

Case: Environmental Monitoring System

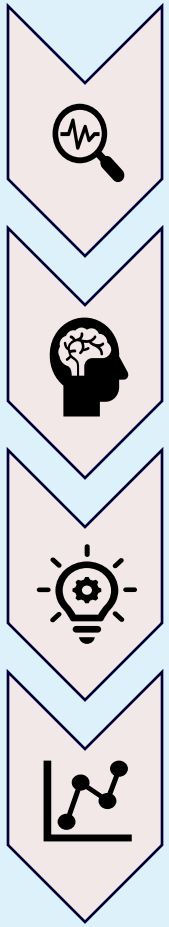
Analysis Approach: PI vs Seeq

Analysis Results / Actions

Summary & Conclusions

Sanofi & Seeq

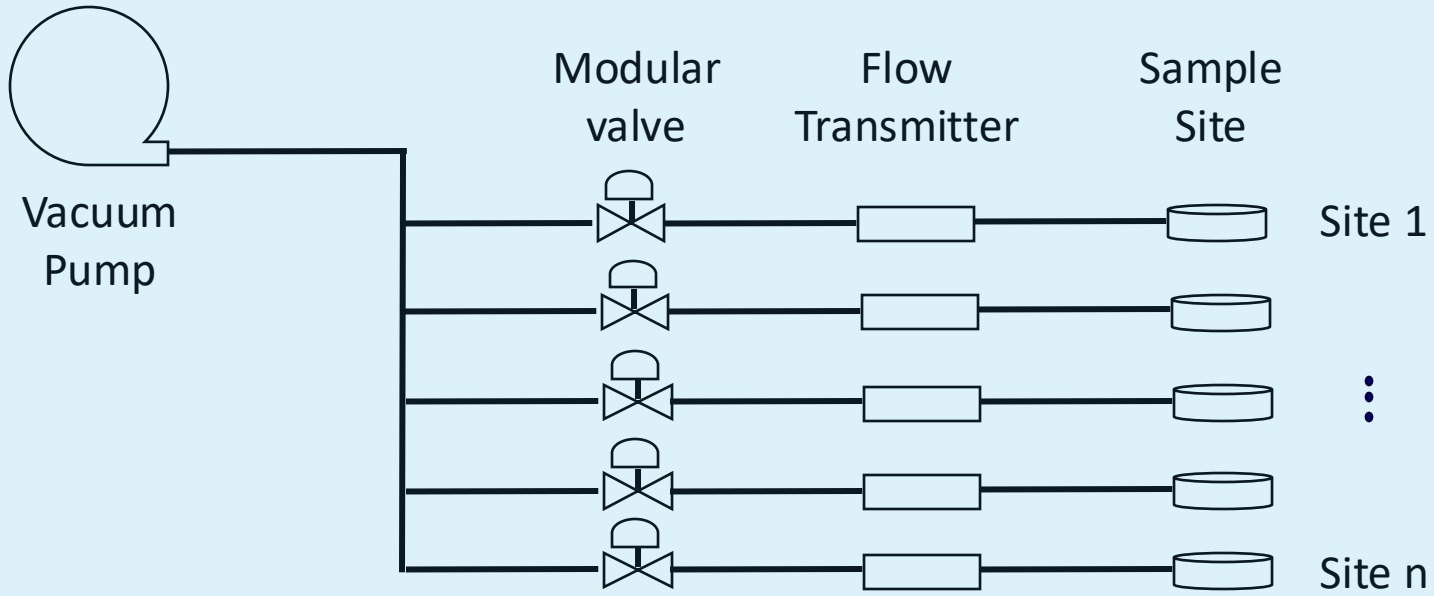
Introduced circa 2021 - Compliment to OSIsoft/Aveva PI



- Troubleshooting & Production Support
- Root Cause Analysis & Deviation Support
- CAPA & Change Controls
- Trending & Predictive Maintenance

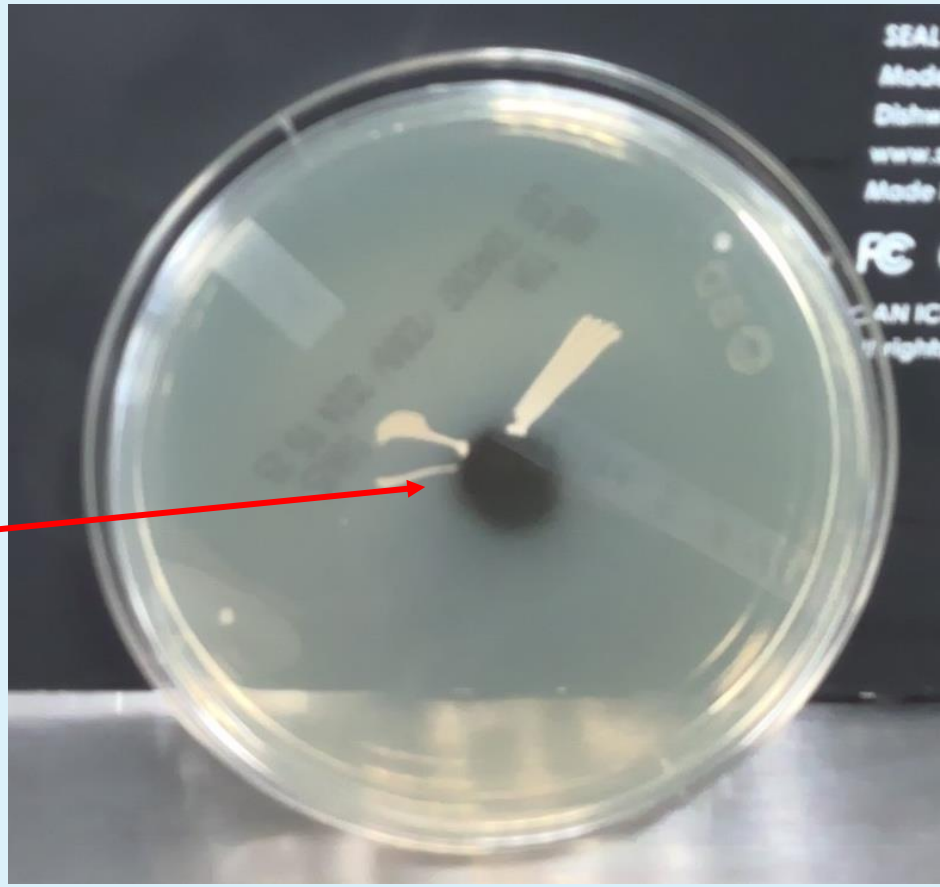
System Background

- Environmental Monitoring System (EMS)
  - **Monitors** critical areas for **viable particulates**
  - Viable air is sampled during active production fills
    - Sample plates are changed out every ~60 minutes
  - Ensures our product is of the highest quality!



The Event – Initial 5W2H

- **W**hat? **Insufficient** vacuum flow rate
  - Discovered a **disconnected tubing**
- **W**here? Viable sampling site – stopper bowl
- **W**ho? Operations and Maintenance
- **W**hen? 08 Mar 2024
- **H**ow? Sample plate lacking "dimple"



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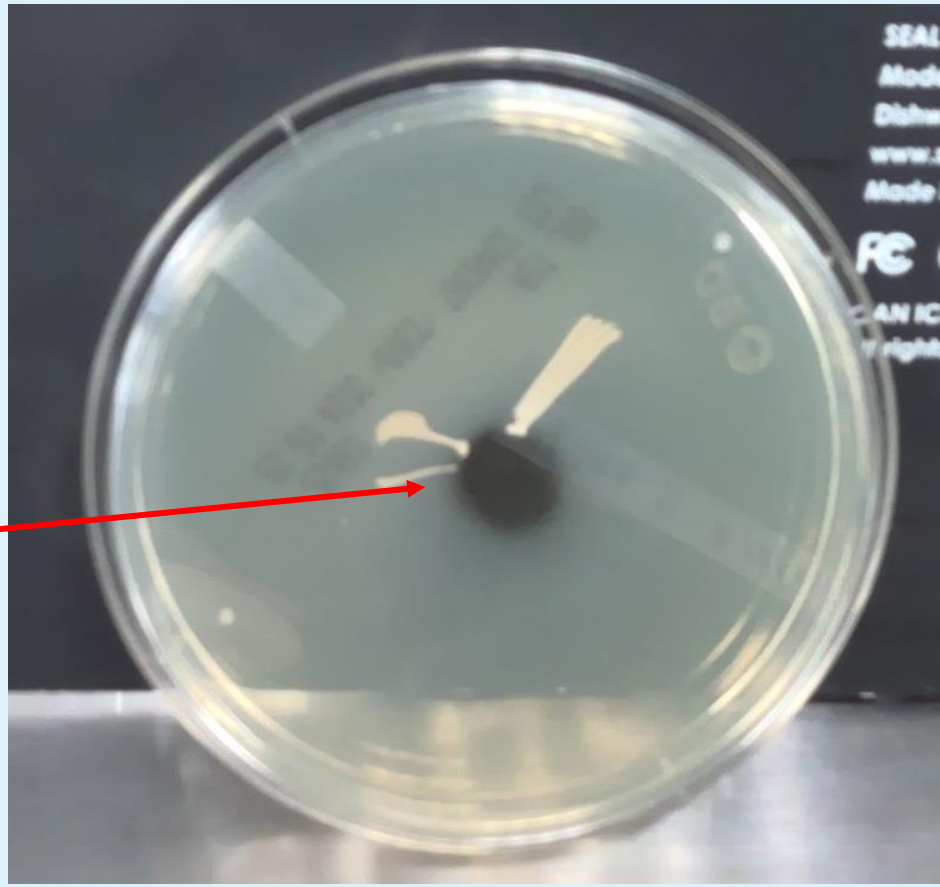
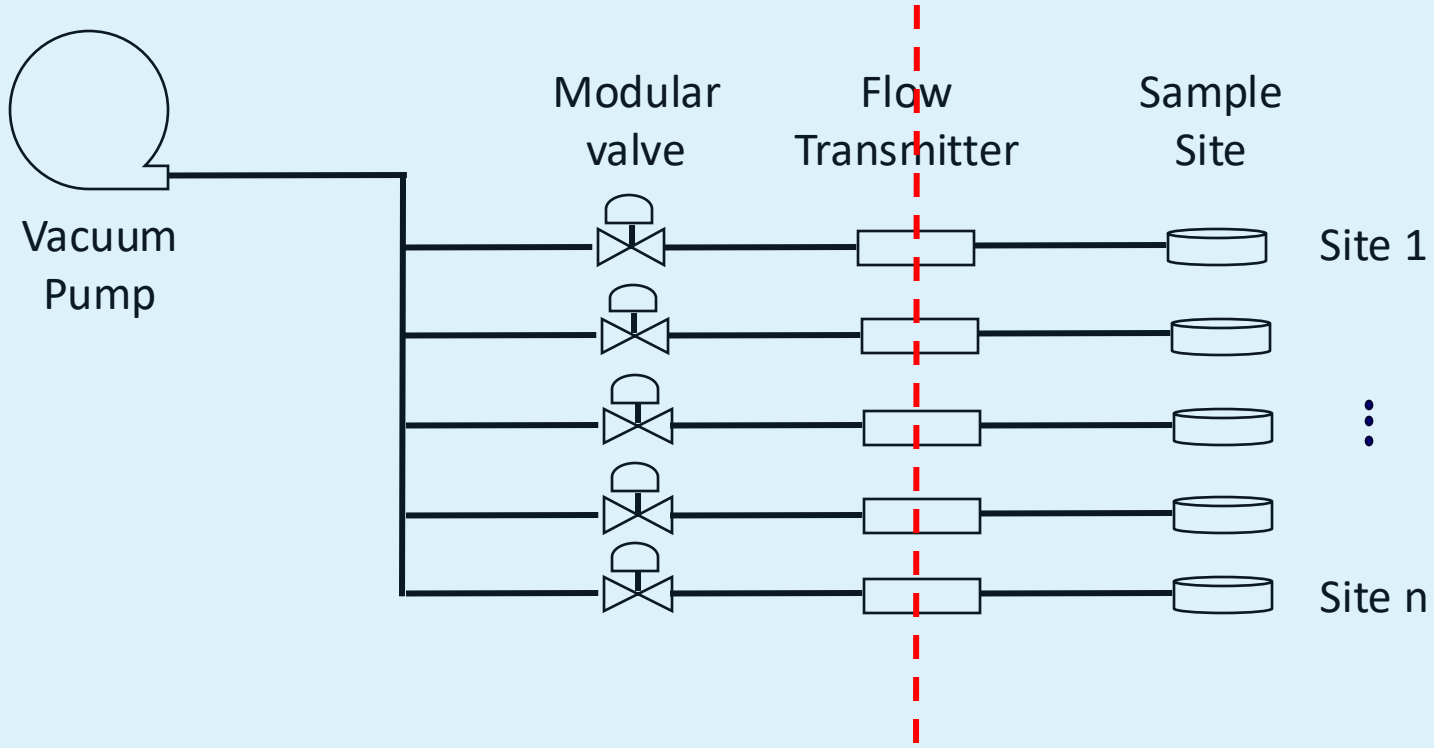


- Key Questions
  - **W**hy?
  - **H**ow Much/How Often/How Long Ago?

Question

- Where would you **prefer** the tubing to have been disconnected? AND
- Where do you think it **actually** did?



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- Where would you prefer the tubing to have been disconnected? AND
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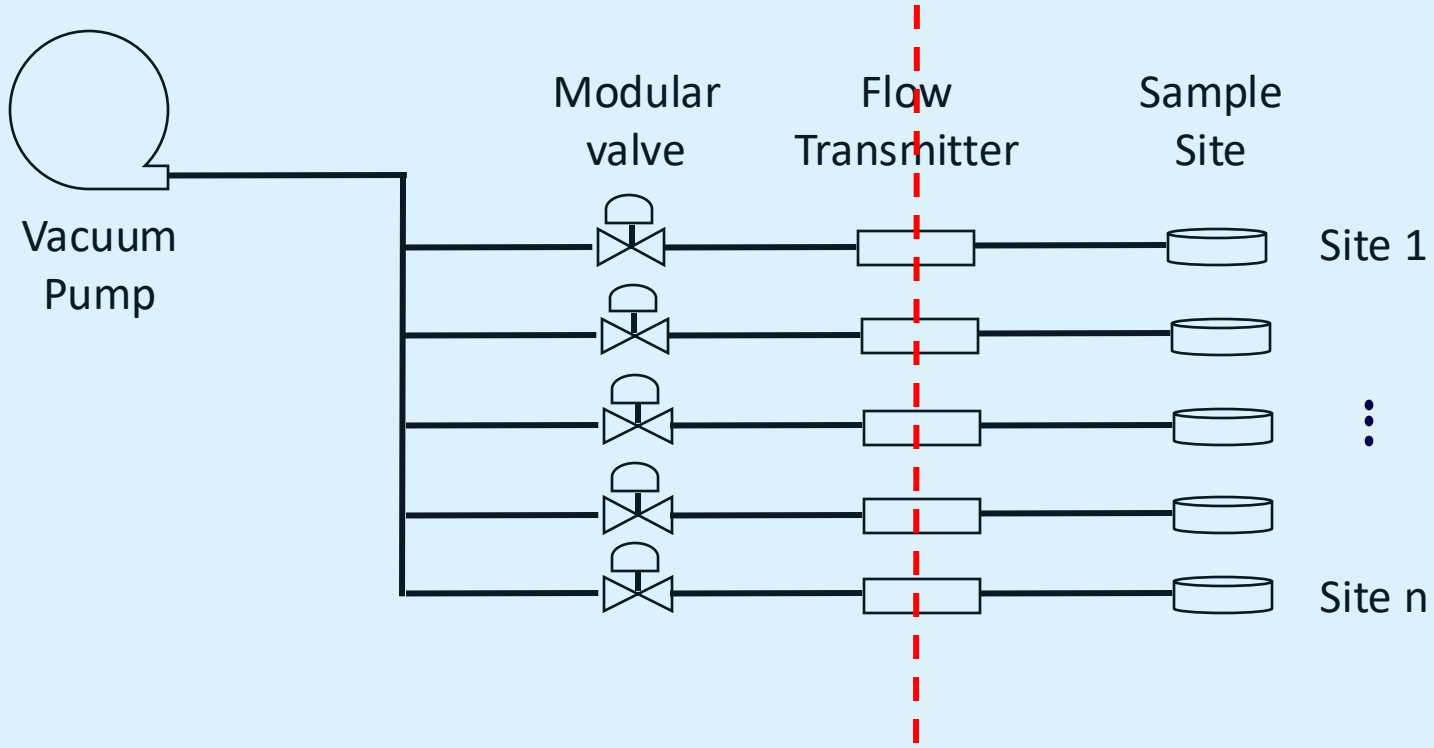

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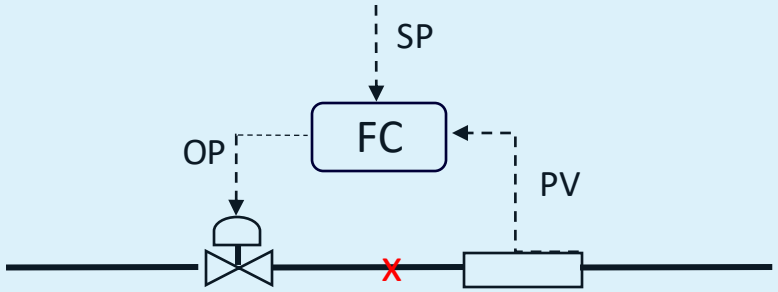

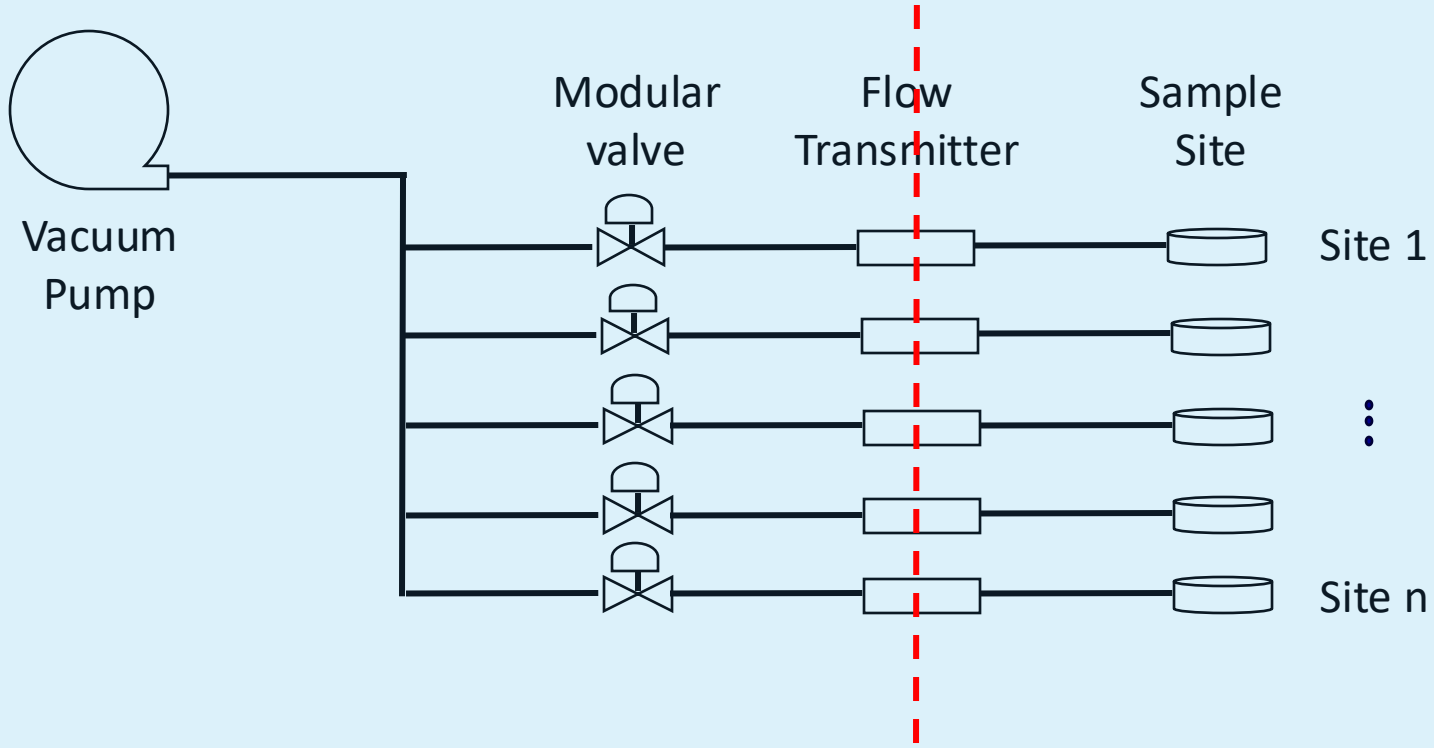

Disconnect: Upstream

- Flow Transmitter = 0 LPM (SS)
- Mod. Valve pos = 100% open

Question

- Where would you prefer the tubing to have been disconnected? AND
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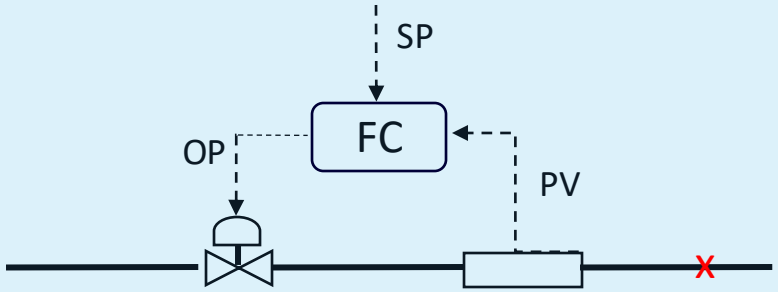

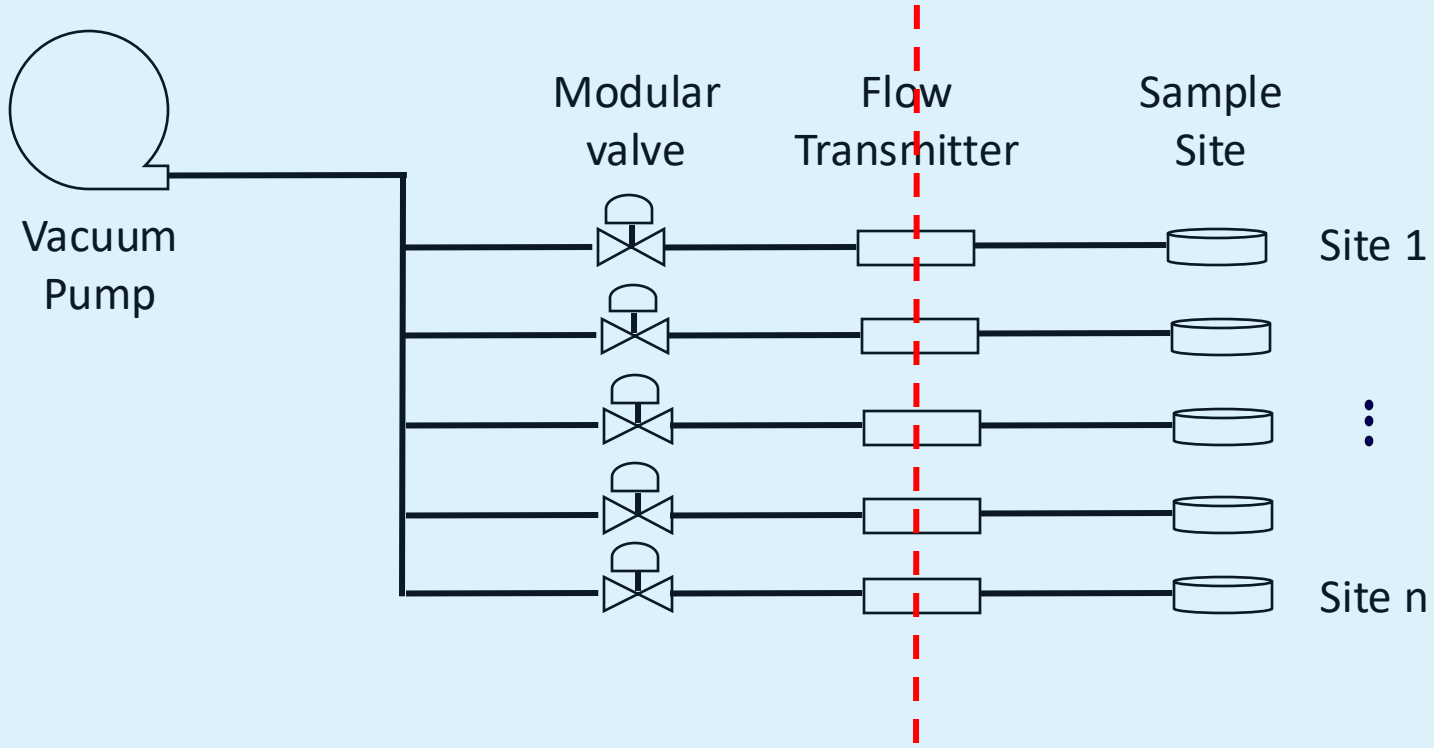

Disconnect: Upstream
- Flow Transmitter = 0 LPM (SS)
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Disconnect: Downstream
- Flow Transmitter = SP (SS)
- Mod. Valve pos = %

Question

- Where would you prefer the tubing to have been disconnected? AND
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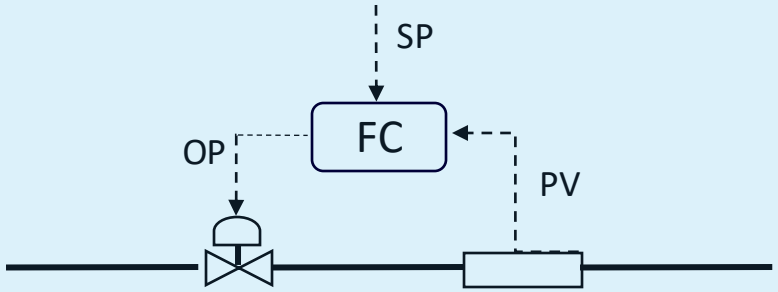
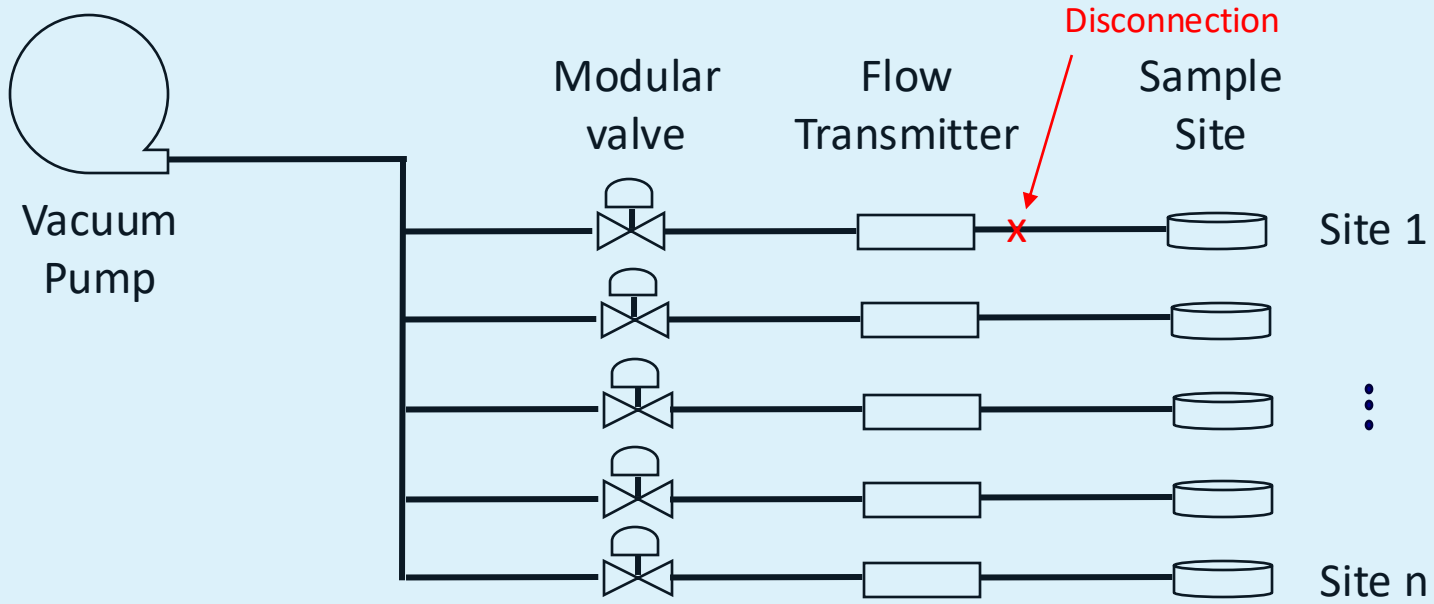
  - Vacuum **flow rate** is controlled via **PID loop**





Disconnect: Upstream
- Flow Transmitter = 0 LPM (SS)
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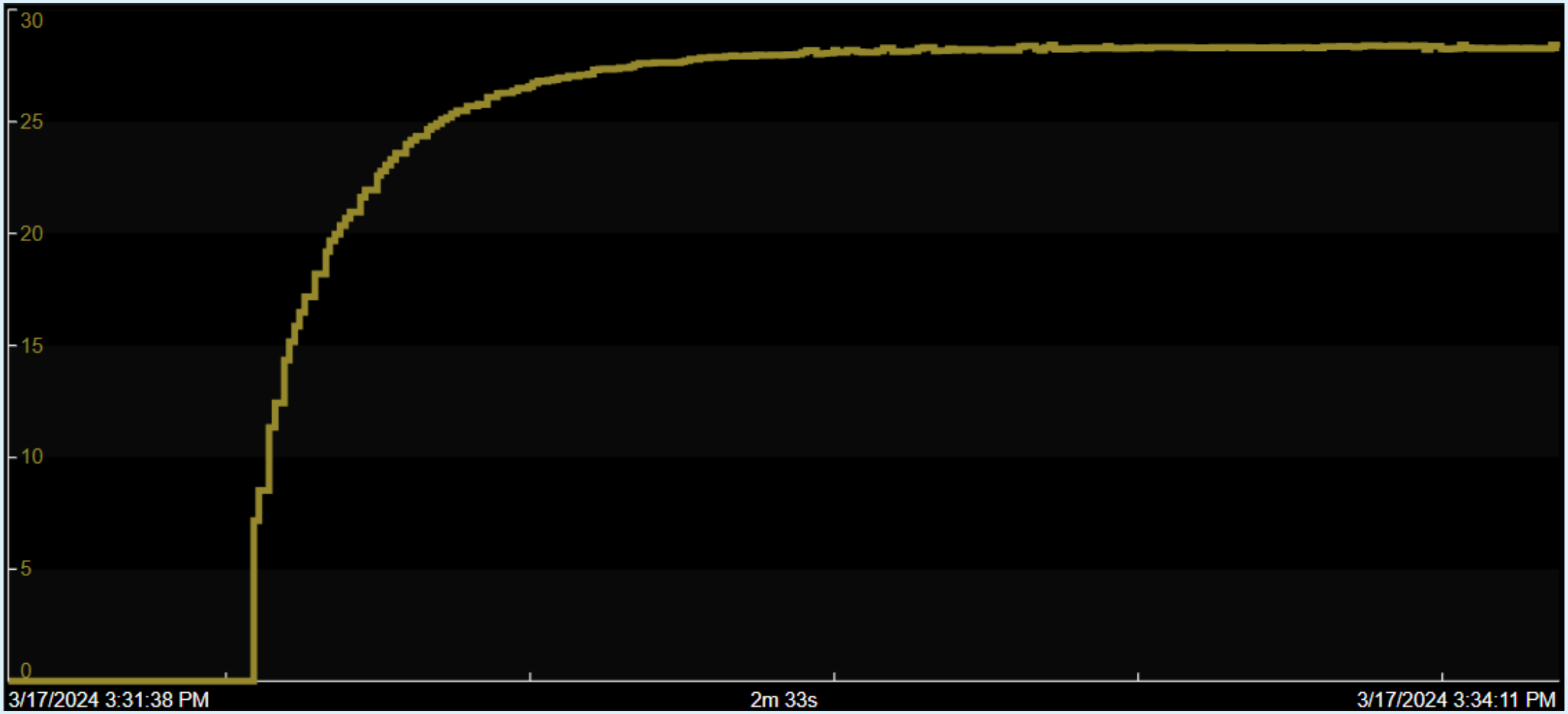
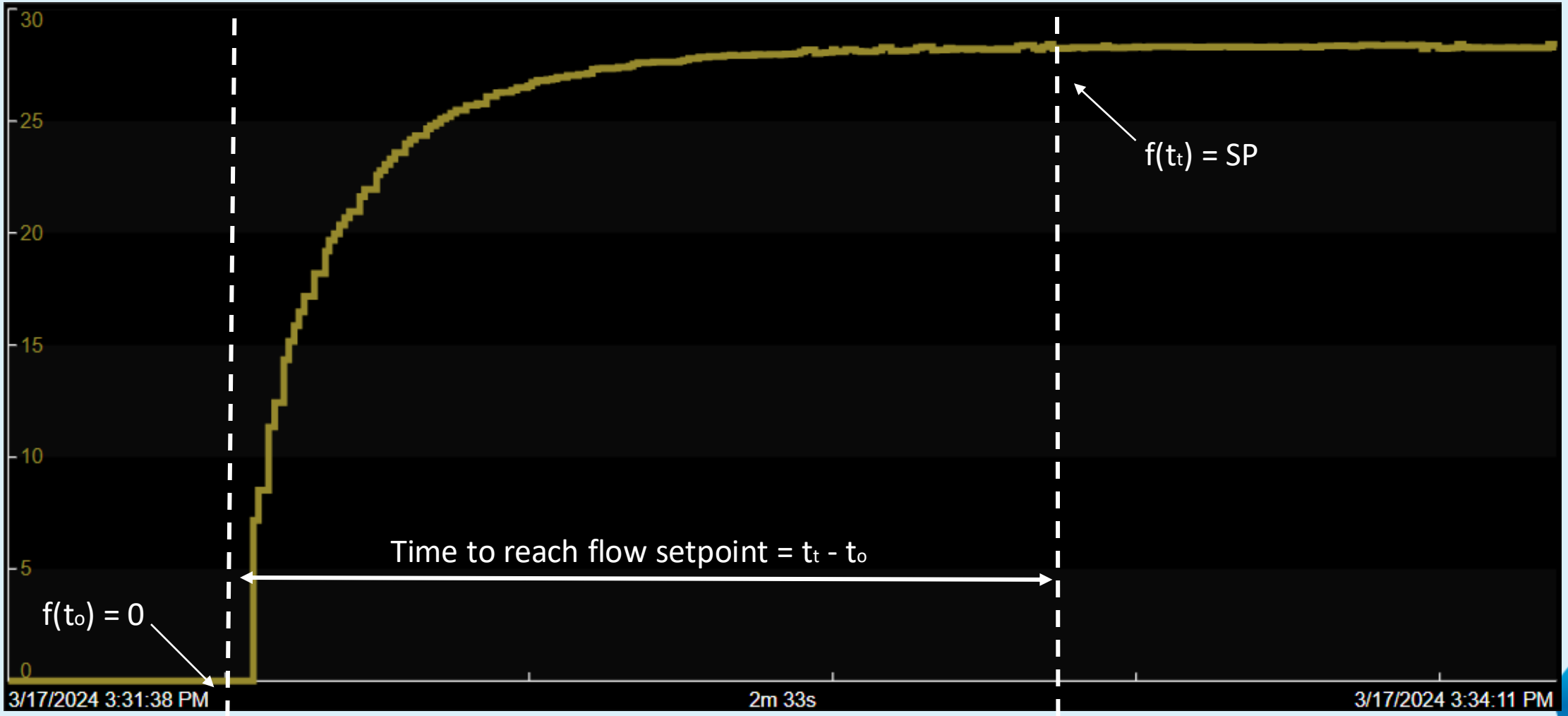
Disconnect: Downstream
- Flow Transmitter = SP (SS)
- Mod. Valve pos = %

Flow Rate (LPM) – one sample period (PI)

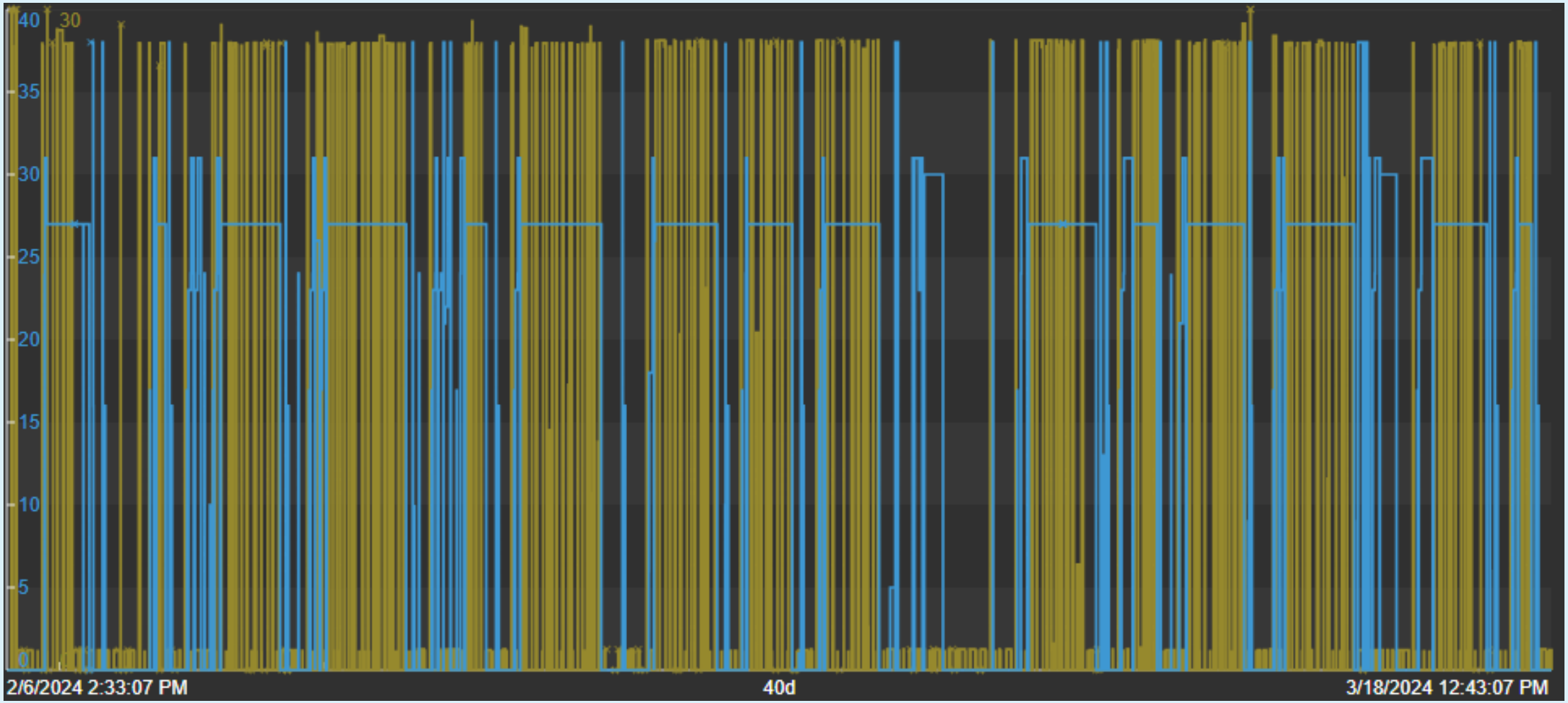


Analysis Approach (PI)

Hypothesis: The time to reach setpoint disconnected < connected

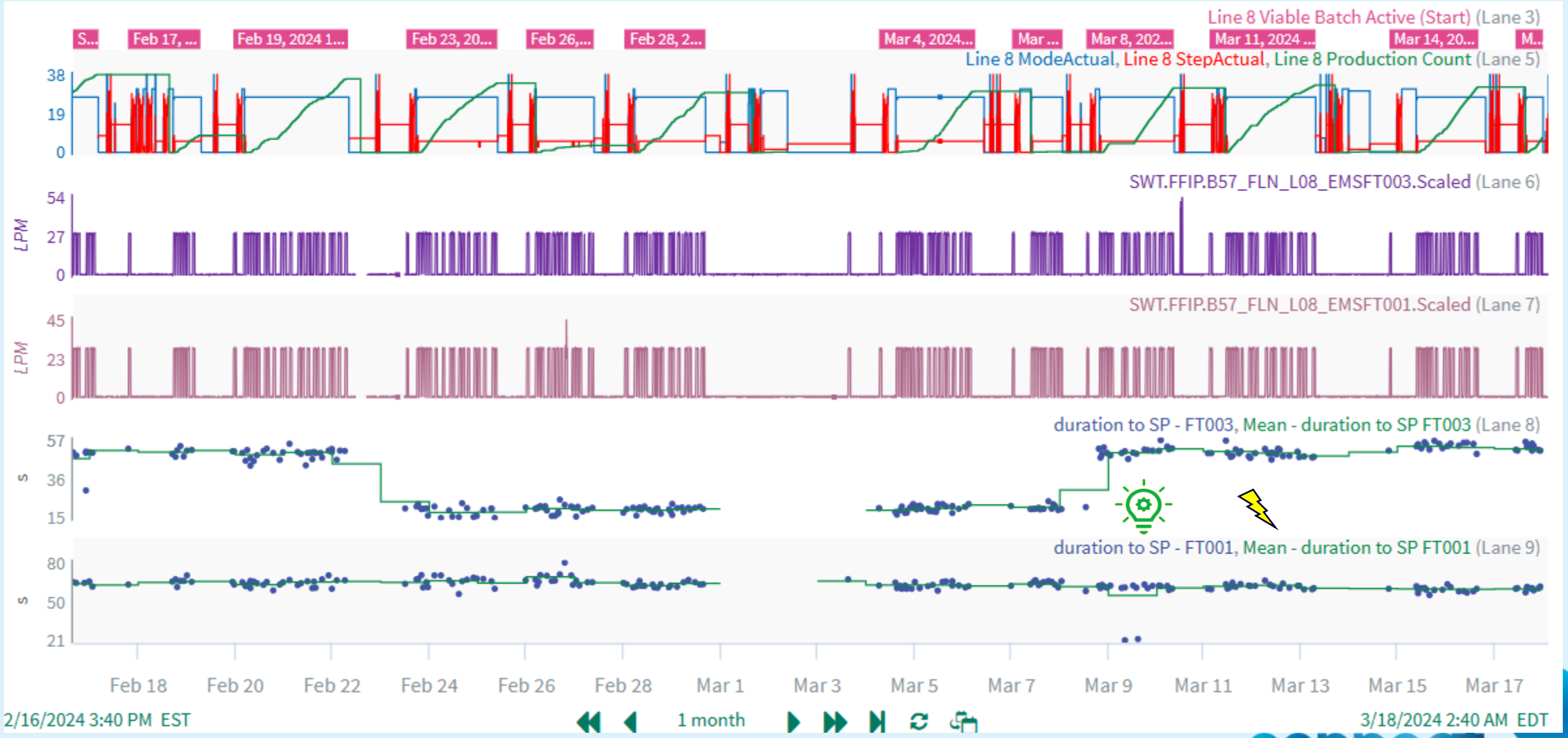


PI Analysis – 1.5 months

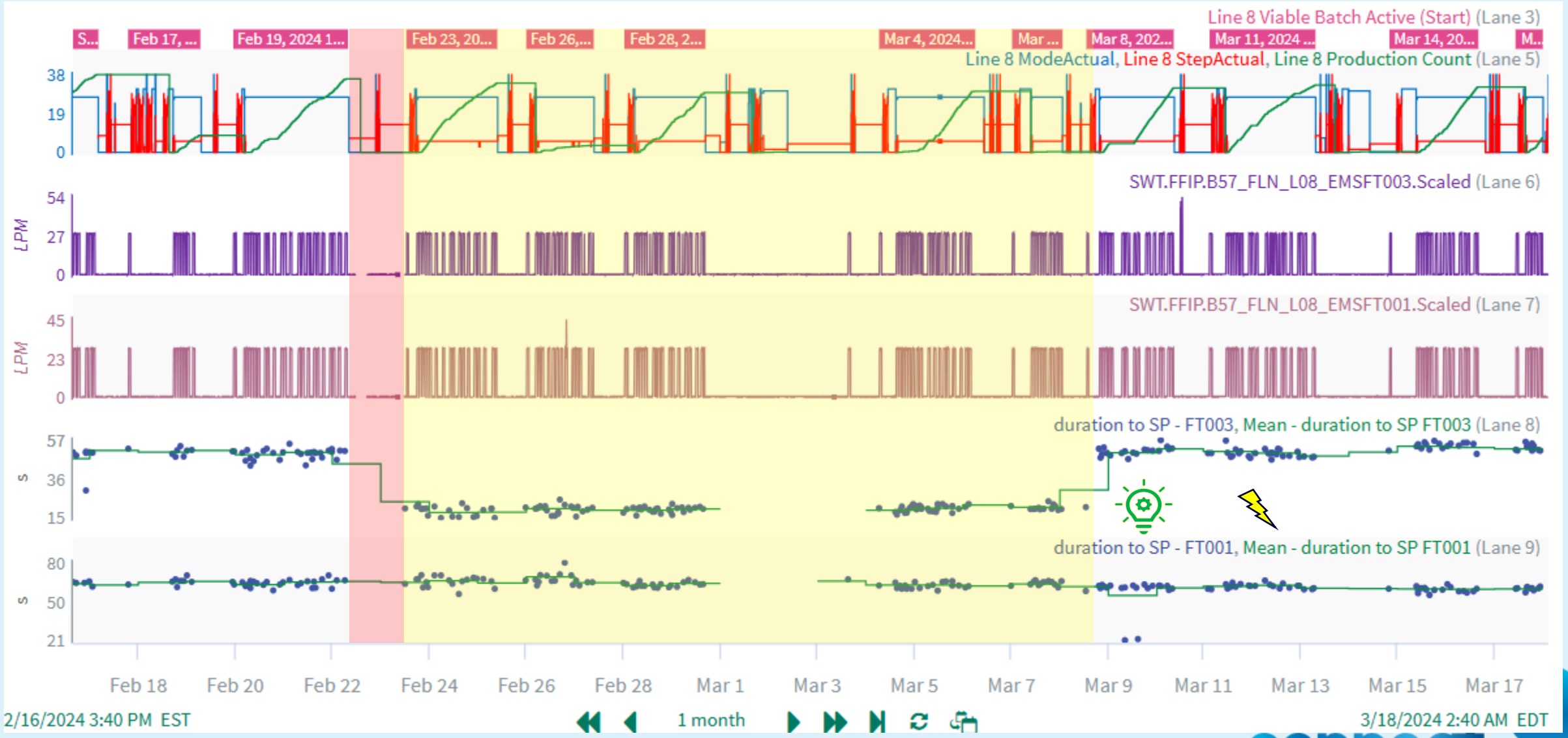


Seeq Analysis – Potential Batch Impact

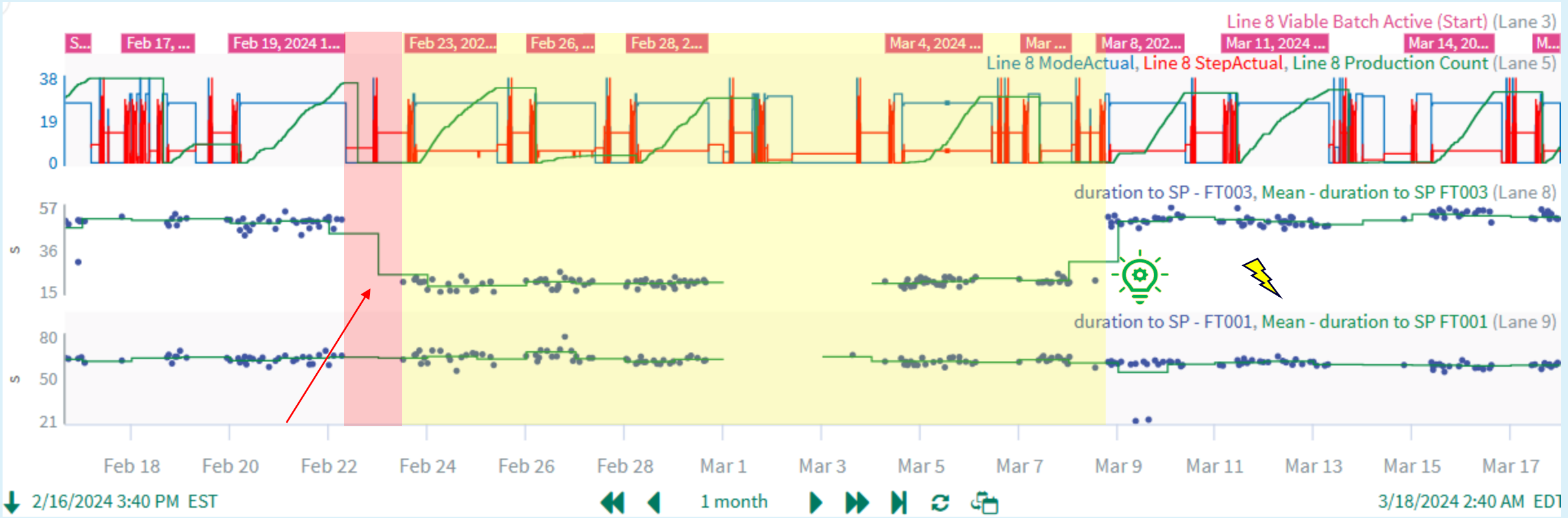
Seeq Analysis – 1 month



Seeq Analysis – Key Dates



Seeq Analysis - Discoveries



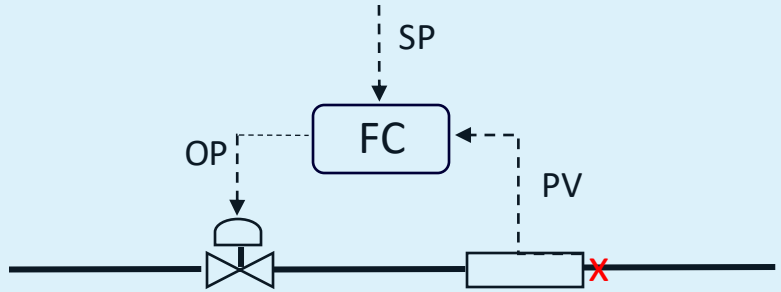
23 Feb 2024 – Work order maintenance intervention where the tubing was disconnected (Why? of 5W2H)

08 Mar 2024 – Event discovered and tubing reconnected (Corrective Action)

Post analysis – 6 batches held from lot release for risk assessment (How Long/How Many? of 5W2H)

Long Term Solutions

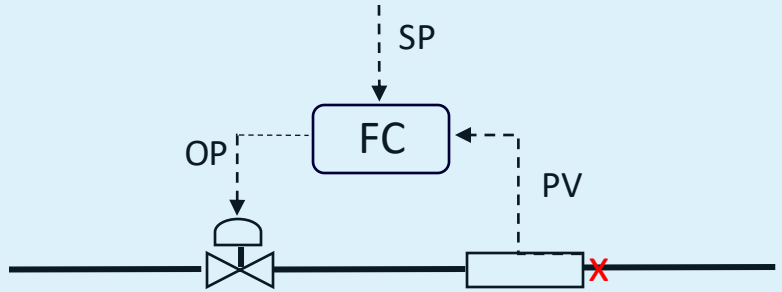
- **Addt'l alarm** to identify future tubing disconnects
  - Valve output adjusts as flow rate changes



- Flow rate PV decreases, valve OP increases
- Flow rate PV increases, valve OP decreases

Long Term Solutions – Increase Detectability

- **Addt'l alarm** to identify future tubing disconnects
  - Valve output adjusts as flow rate changes
  - If tubing disconnects, PV **increases**
  - Increasing PV, valve OP **decreases**
  - **Alarm implementation:**
    - If valve **OP% < limit**, then trigger alarm



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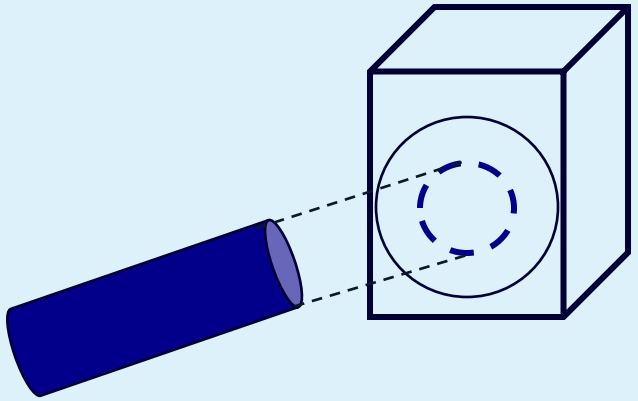
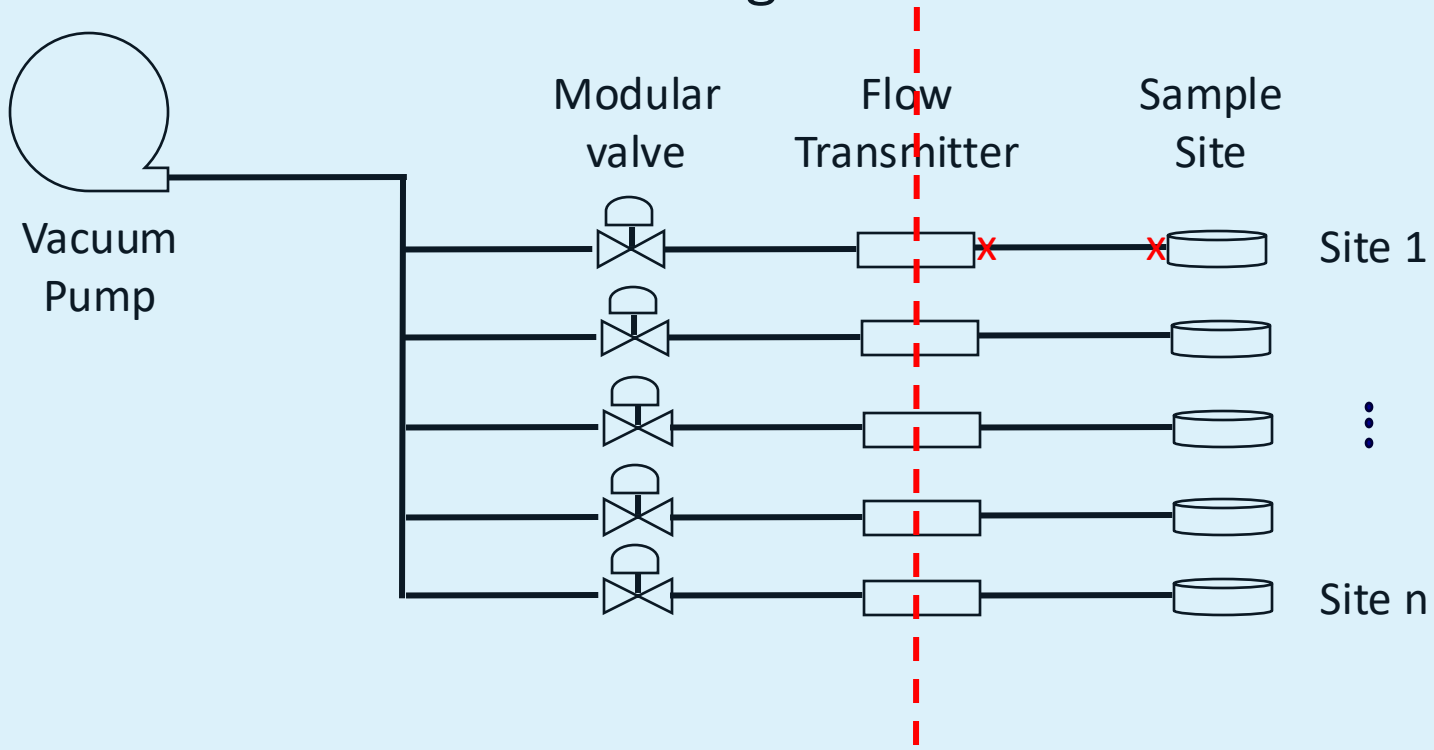


Long Term Solutions – System Redesign

- **Addt'l alarm** to identify future tubing disconnects
- **Move** the flow transmitters **closer to the point of sample**
  - **Reduces** amount of tubing that could be compromised **downstream** of the flow transmitter
  - **Reduces** number of tubing disconnects that are **less detectable**



Summary

Troubleshooting & Production Support	Point of Disconnect Determination
Root Cause Analysis & Deviation Support	Complete 5W2H Why? & How many (batches)?
CAPA & Change Controls	Tubing Disconnect Alarm System Redesign – sensor relocation
Trending & Predictive Maintenance	Six Sigma Run Chart – Time to SP

Thank You!

Contact: Kevin Louie

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THANK YOU!