Strategies for Monitoring and Troubleshooting Biopharmaceutical Manufacturing Operations

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Strategies for Monitoring and Troubleshooting Biopharmaceutical Manufacturing Operations

OUTLINE

- Assessing the Data Bottleneck for a Process
- Statistical Process Control Case Study
- Chromatography Troubleshooting Approaches
- Five Keys to Successful Process Data Systems

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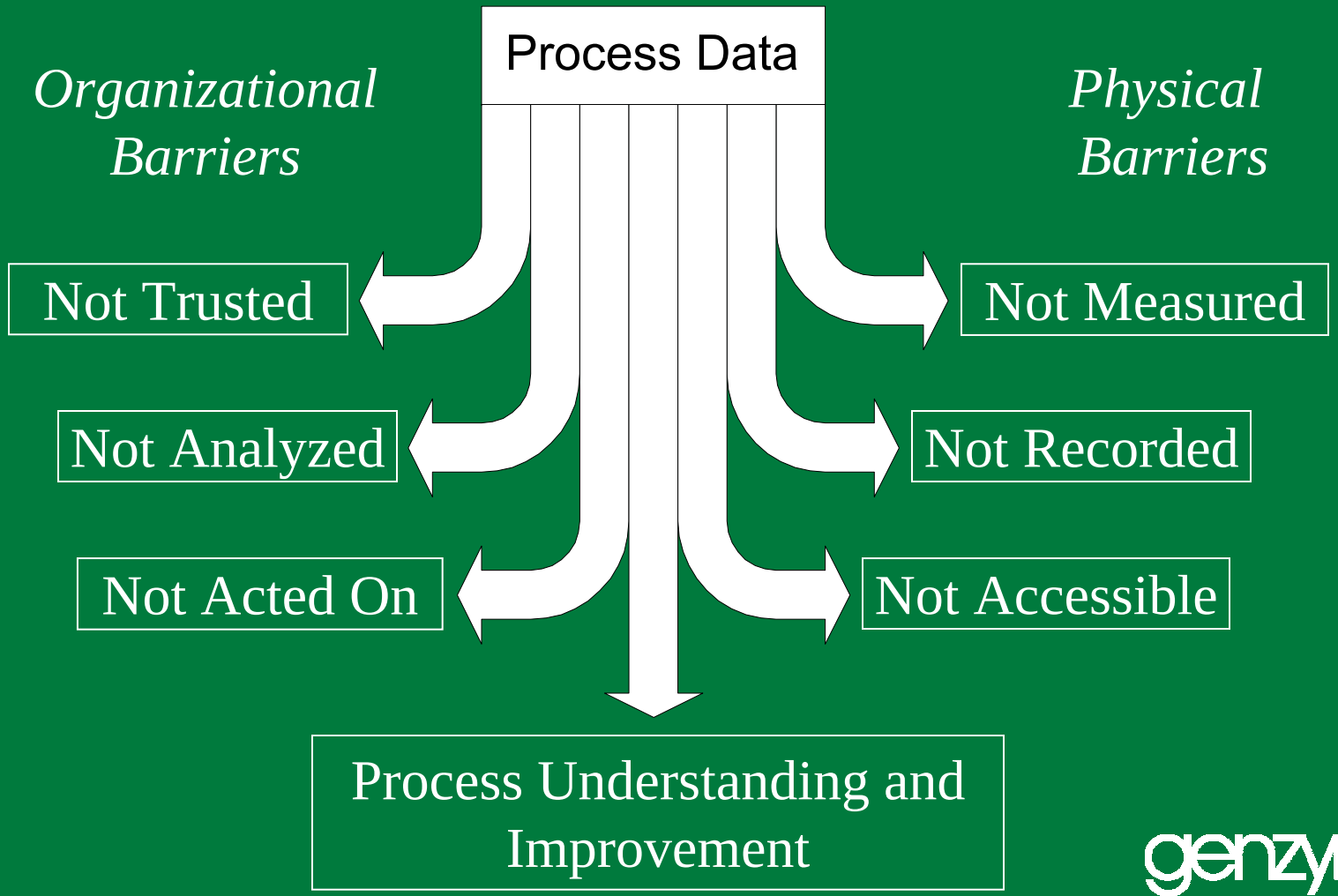
Assessing the Data Bottleneck for a Process

What hinders improvement/troubleshooting most?



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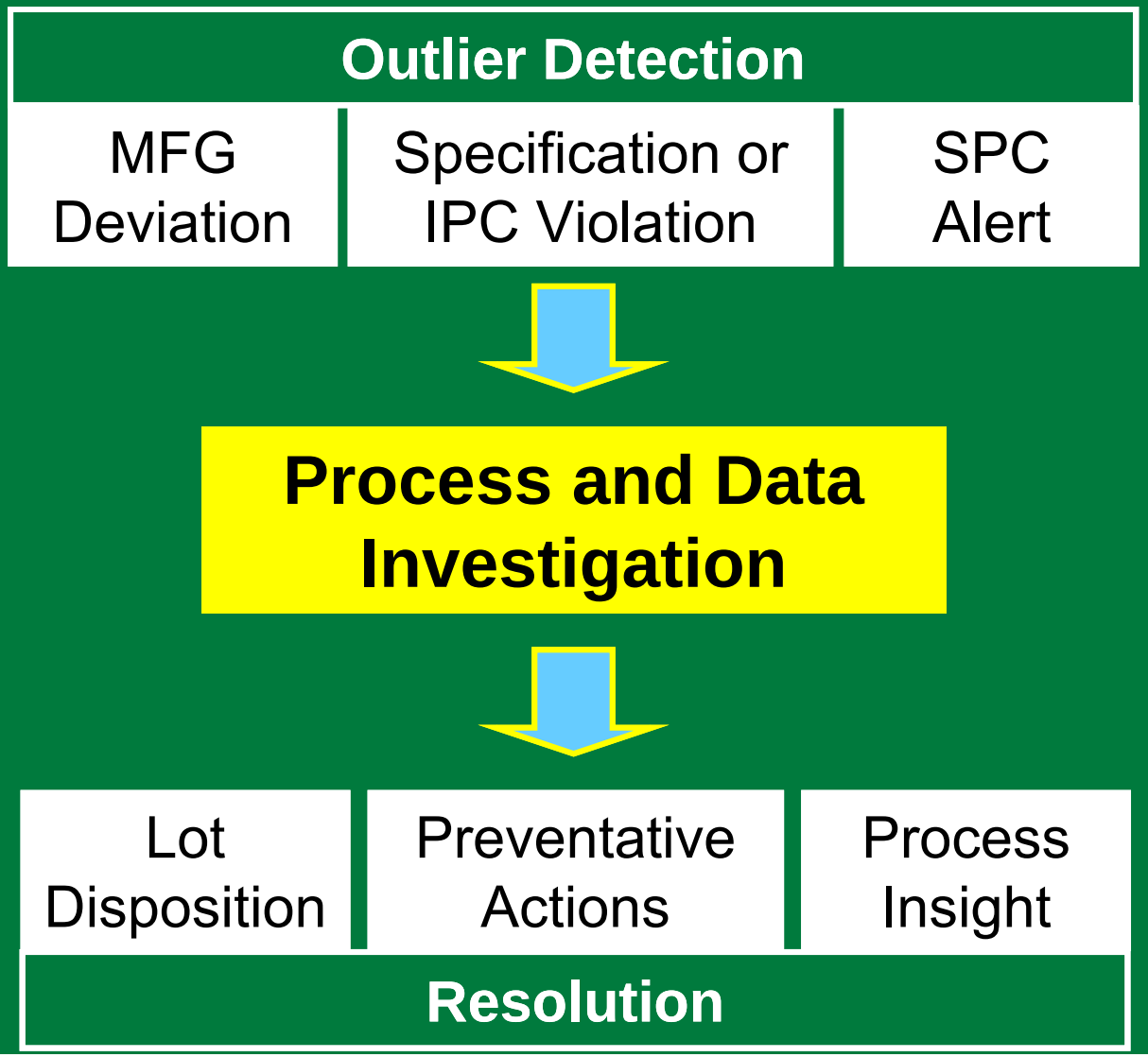
Process Troubleshooting Overview



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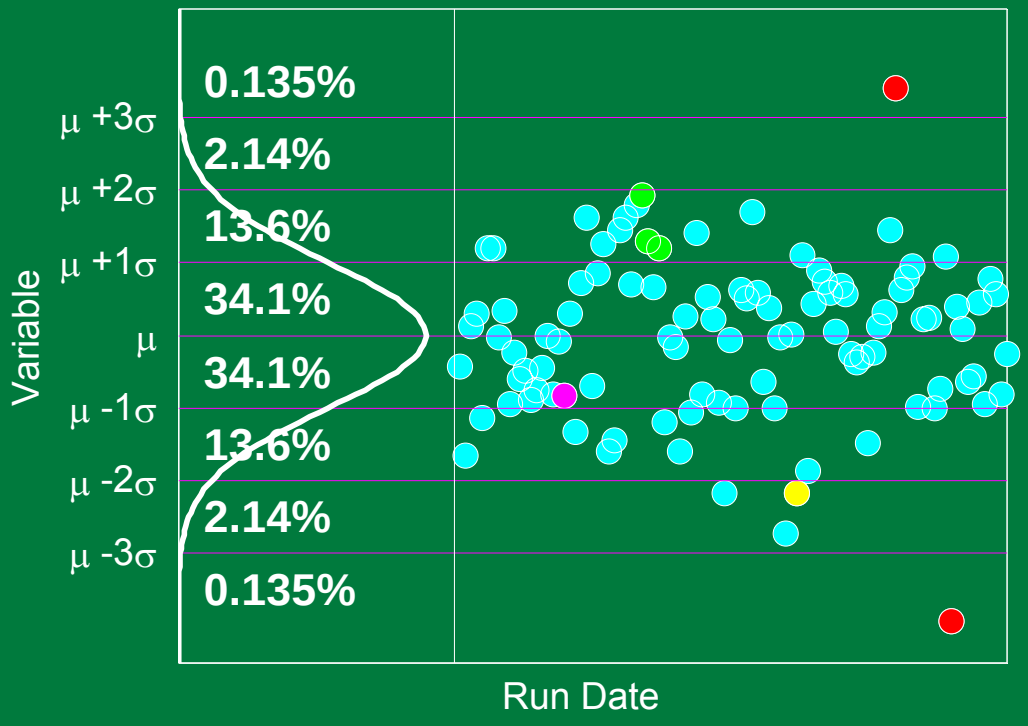
How to Monitor Large Quantities of Data?
->*Statistical Process Control Rules*



Western Electric Rules

- 1 outside 3 σ
- 2 out of 3 outside 2 σ
- 4 out of 5 outside 1 σ
- 8 or more same side of μ

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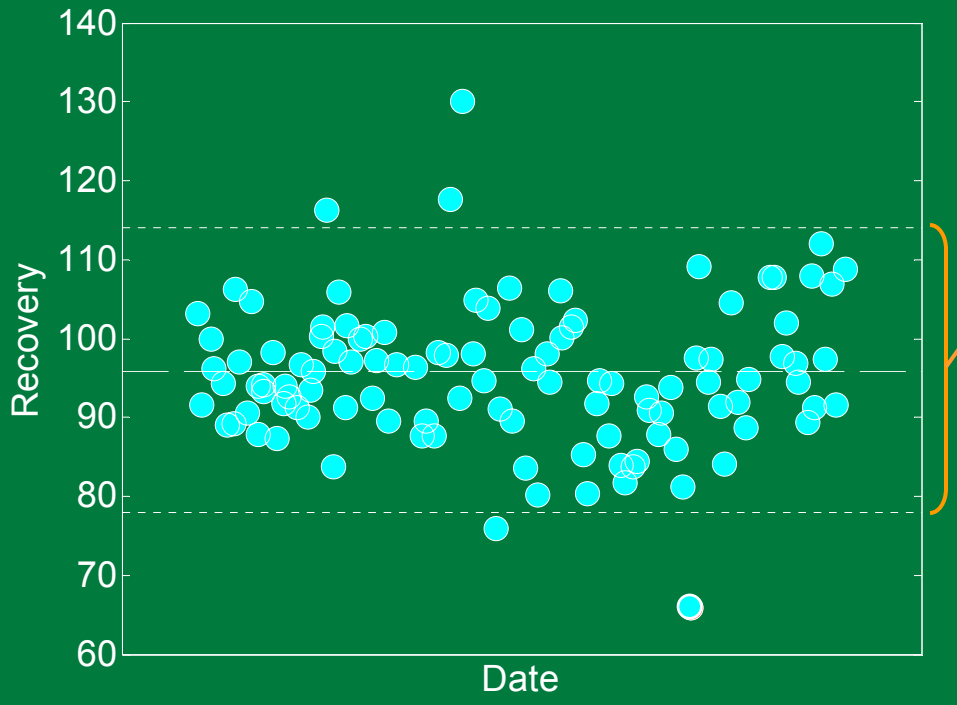
SPC Case Study: Purification Column Recovery



Most data fall within formal alert limits

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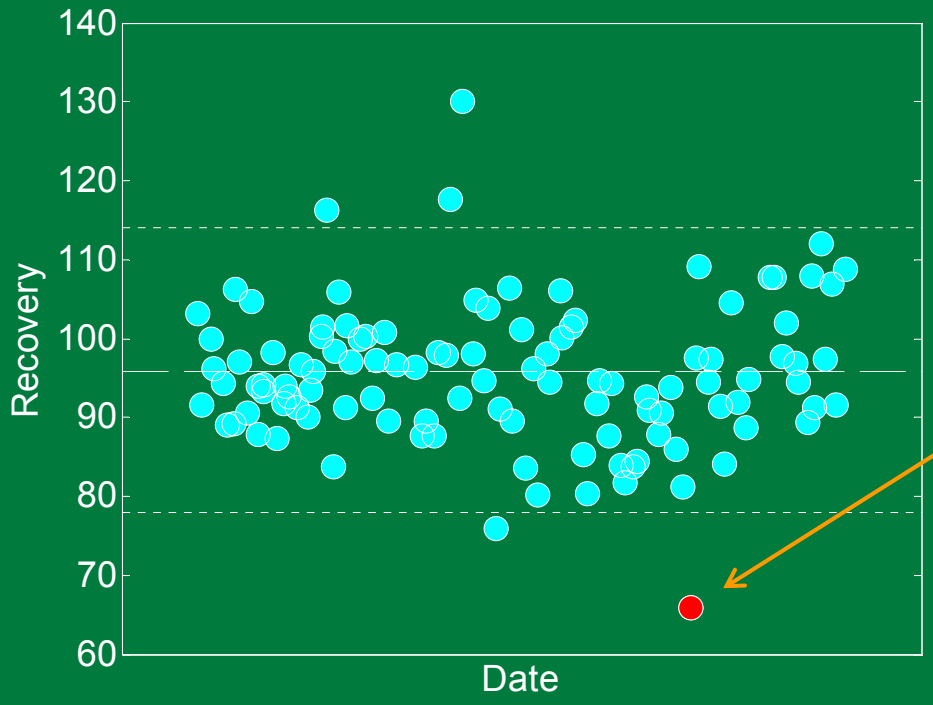
SPC Case Study: Purification Column Recovery



- Most data fell within formal alert limits
- Low recovery triggered formal investigation

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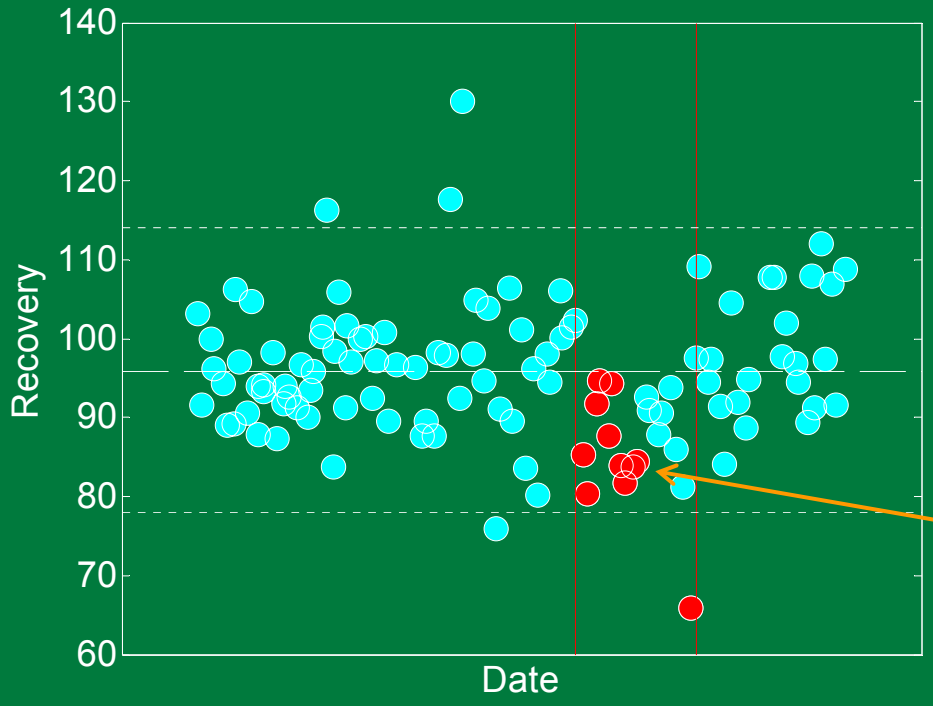
SPC Case Study: Purification Column Recovery



- Most data fell within formal alert limits
- Low recovery triggered formal investigation
- SPC Alert (8 < mean) visible 10 runs earlier
- ~10% of each batch went to drain for 20 batches

Allston Automated SPC System:

- Immediate e-mail notifications
- Hyperlinked trends & lot trees

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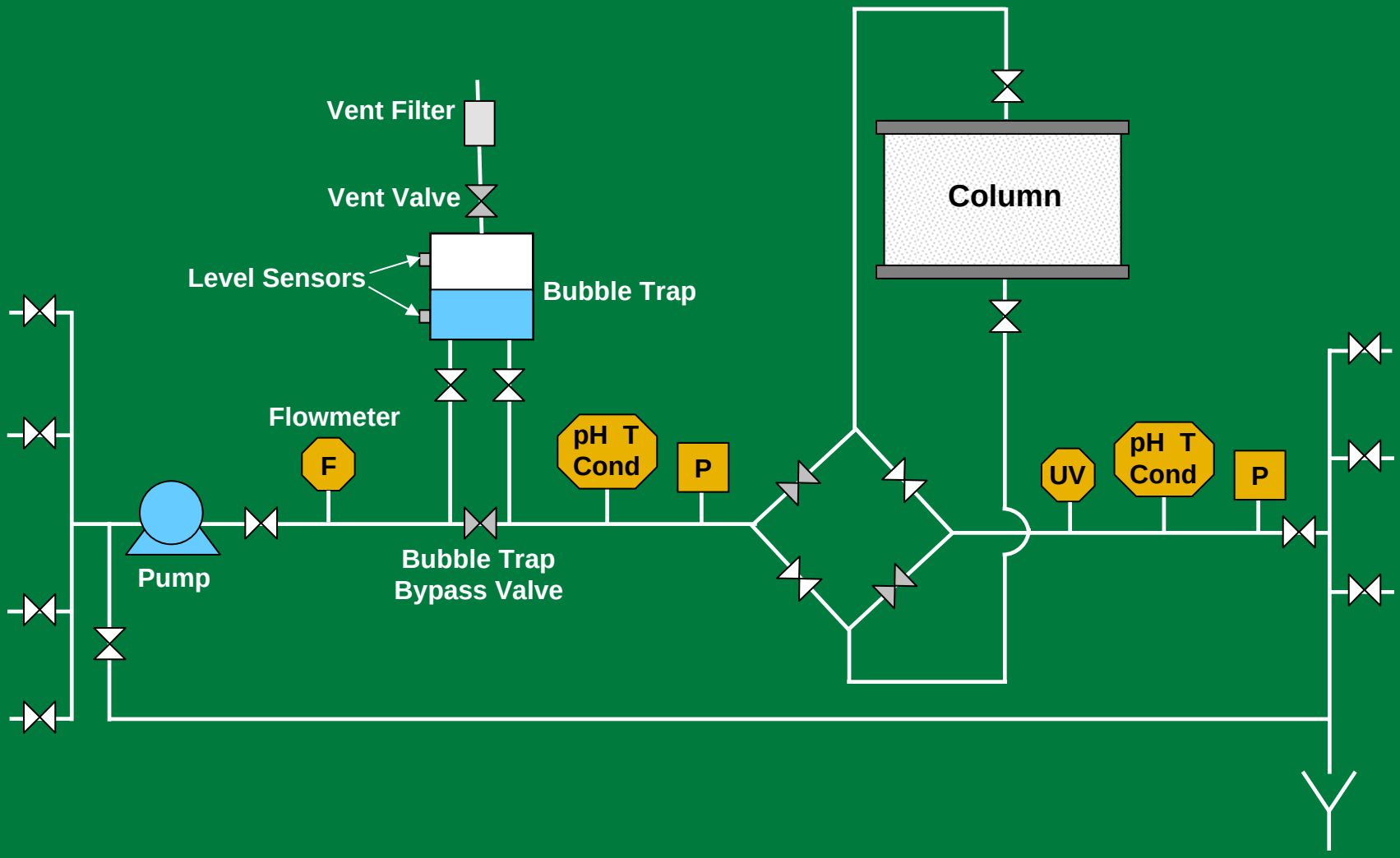
Chromatography System Overview



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What Can Go Wrong in Chromatography?

DATA
- Data entry
- Assay
- Sampling
- Sensor
- Assumptions

EQUIPMENT
- Control system
- Valve leaks
- Bed channeling
- Bed compression
- Other…

60 cm Chromatography Column, Skid, and Piping

PROCESS & MATERIALS
- Mixing
- Material stability
- Precipitation
- Parameter sensitivity
- Procedural gaps
- Operator errors
- Raw material issues

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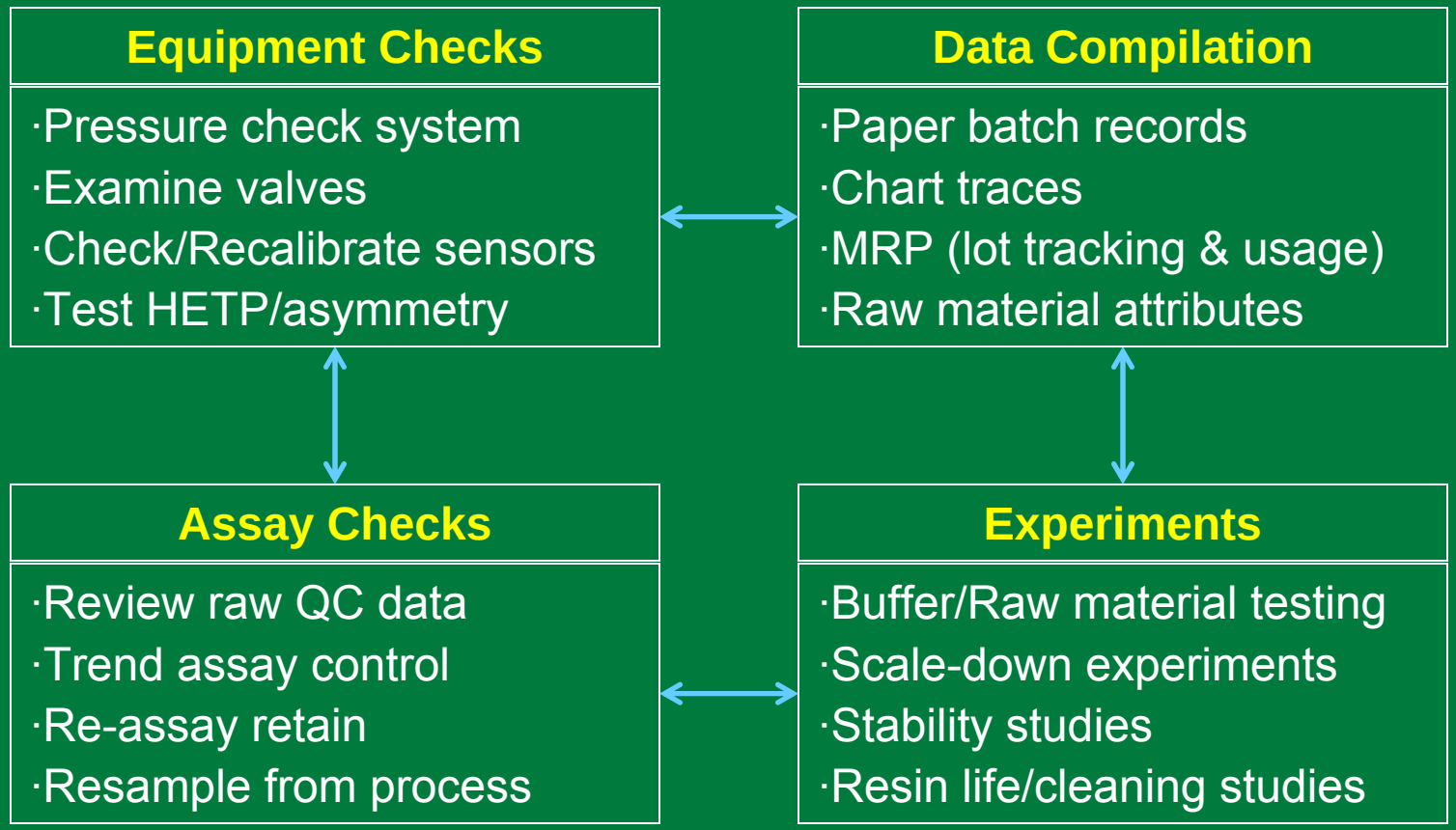
Chromatography Investigative Options



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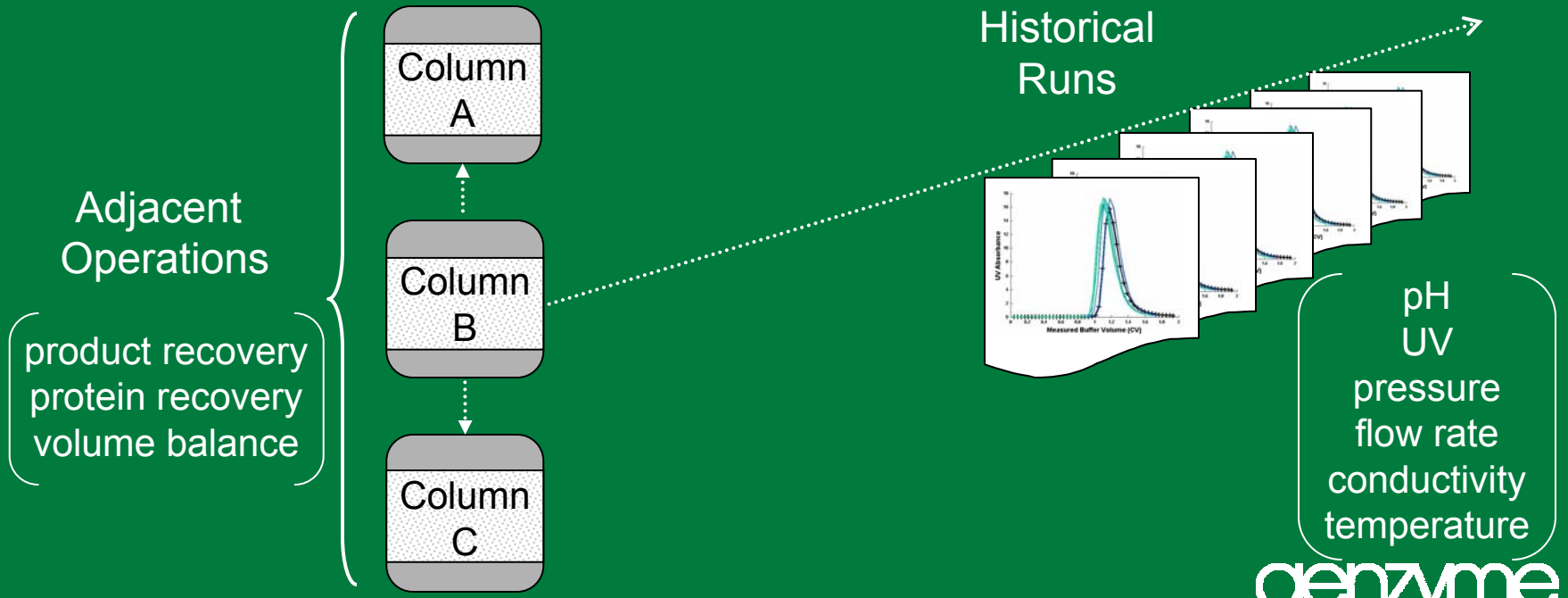
Is Data Consistent with Adjacent Operations and Batches?

Component Balances Across Adjacent Process Operations → Internal Consistency Checks ← Historical Online Profile Comparison



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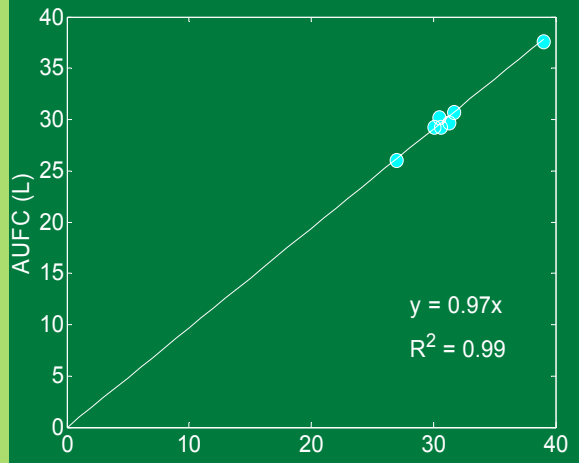
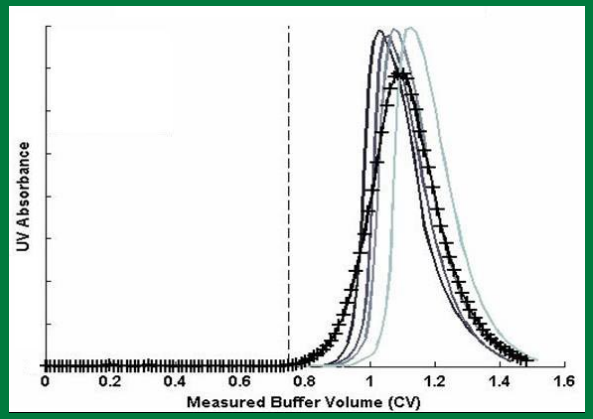
Is Data Internally Consistent?

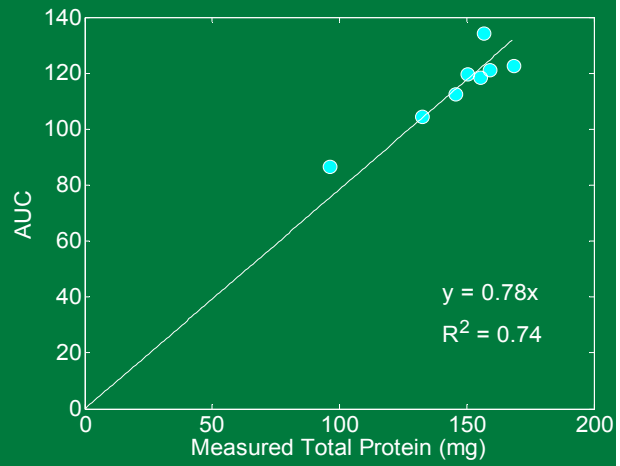
Component Balances Across Adjacent Process Operations → **Internal Consistency Checks** ← Historical Online Profile Comparison



Total Flow vs. Volume



Elution Profile Attributes



Total Protein vs. Area under curve

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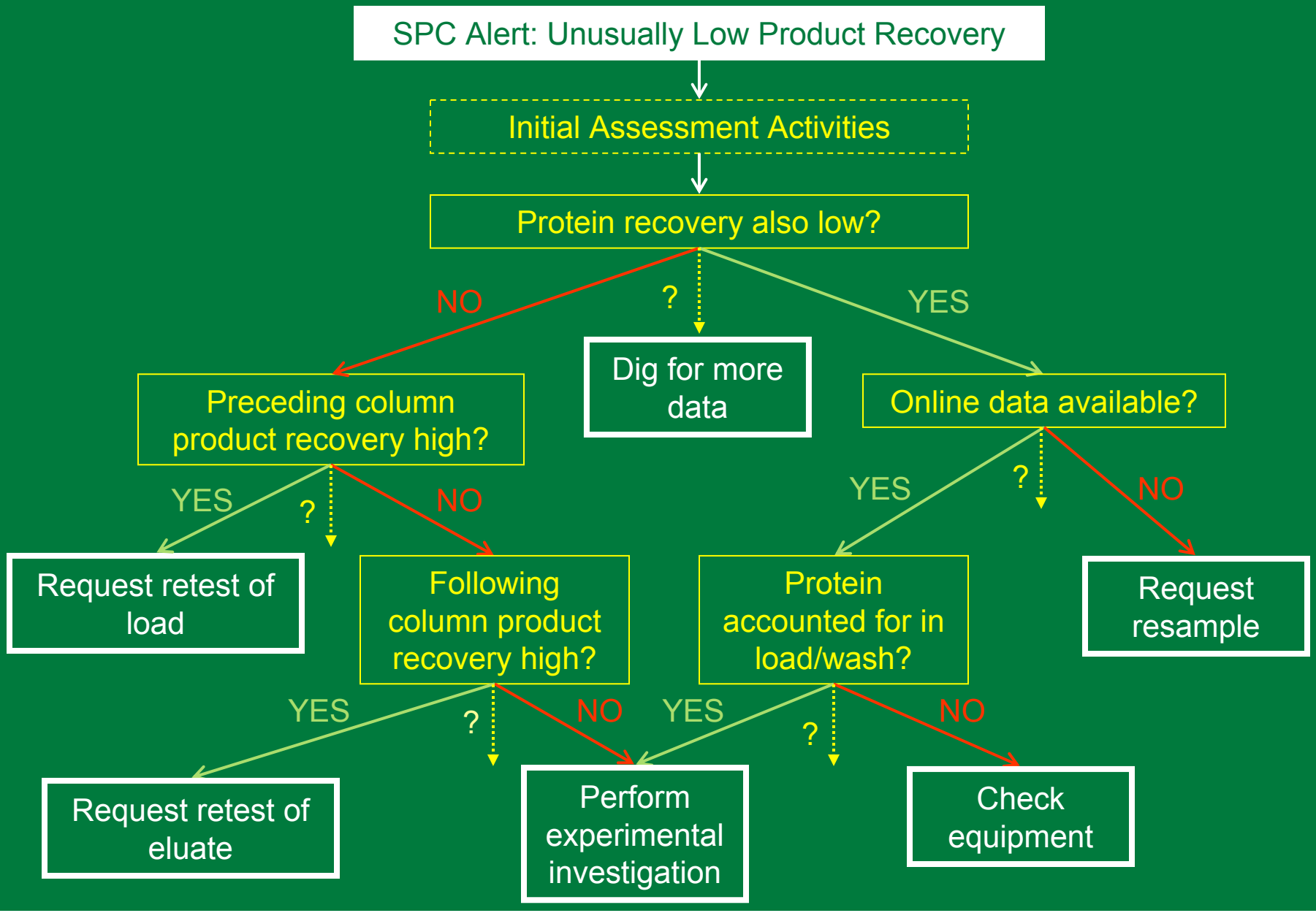
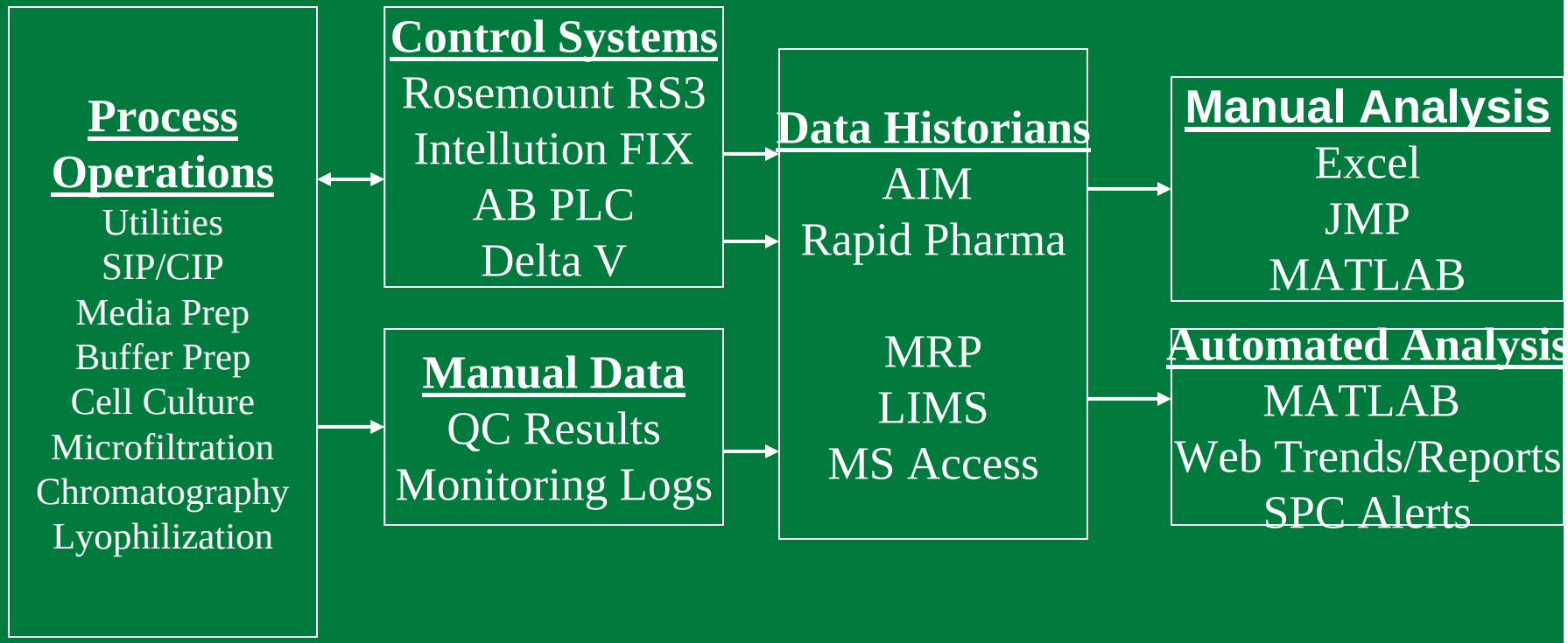
Systematically Choosing Investigative Steps…



Allston Landing Process Data Flows



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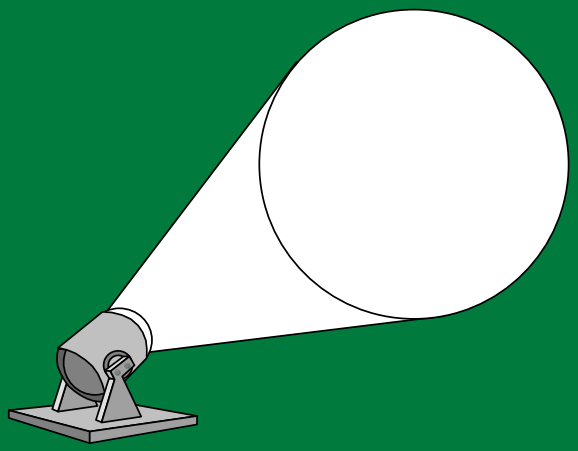
Five Keys to Successful Data-Driven Process Improvement

- #1: Create broad awareness of how the process is running



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Five Keys to Successful Data-Driven Process Improvement

- #2: Ensure manual data entry has both immediate and long-term benefits.

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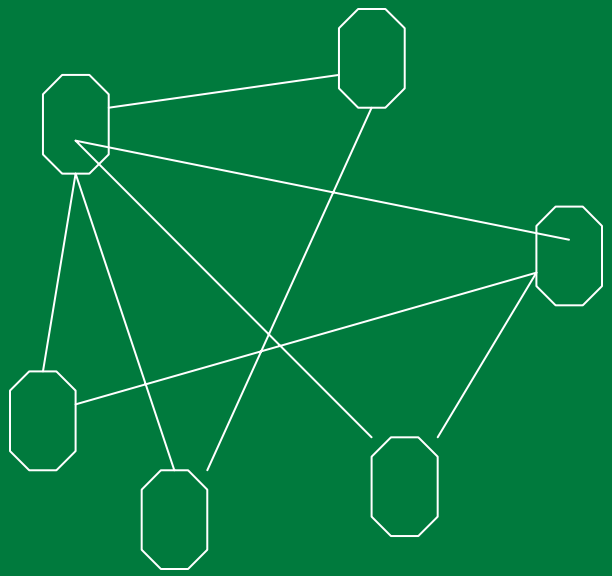
Five Keys to Successful Data-Driven Process Improvement

- #3: Exploit Metcalfe's Law:
  - *the value of a network grows by the square of the number of its users*



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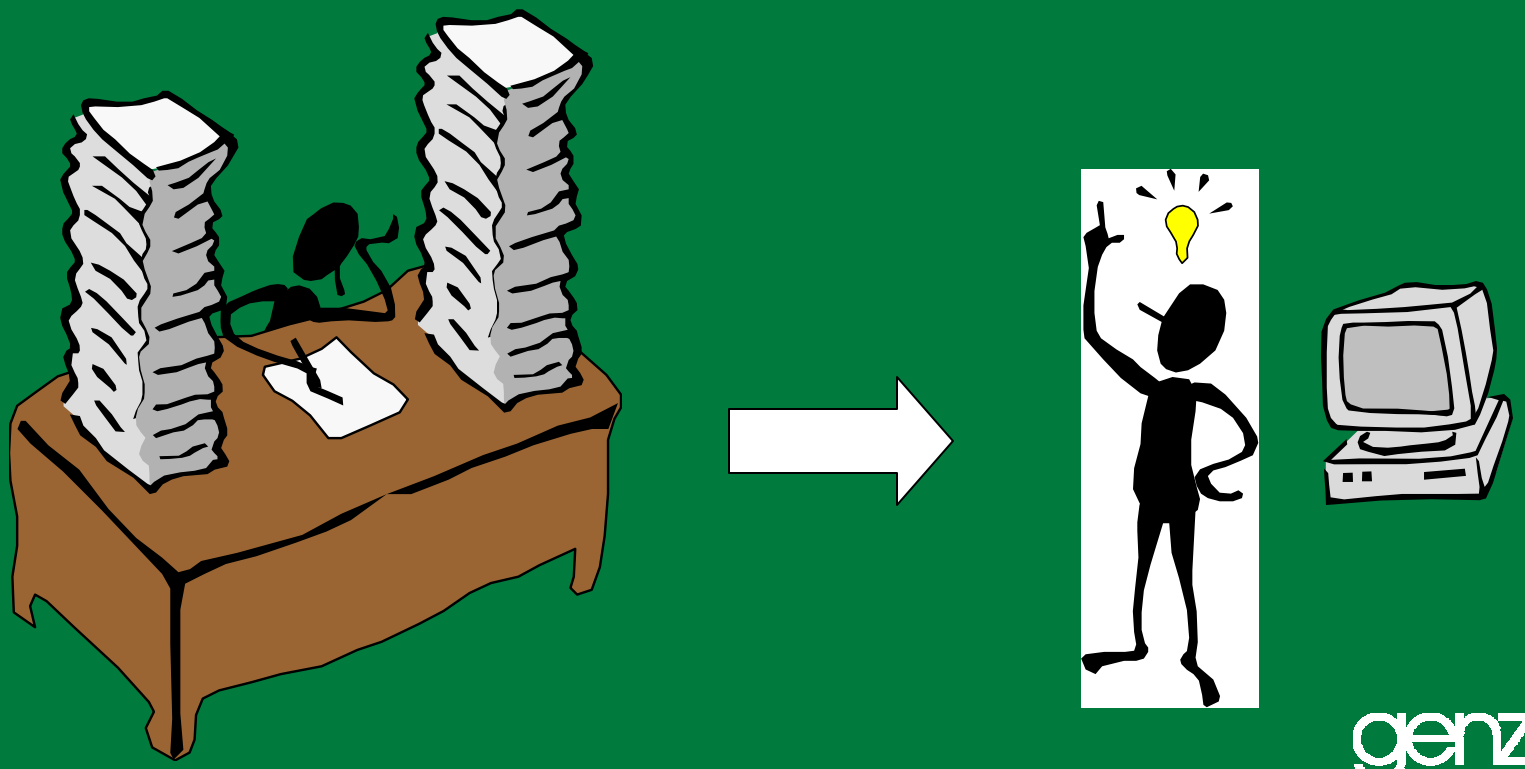
Five Keys to Successful Data-Driven Process Improvement

- #4: Lower barriers (activation energy) to explore ideas and confirm theories



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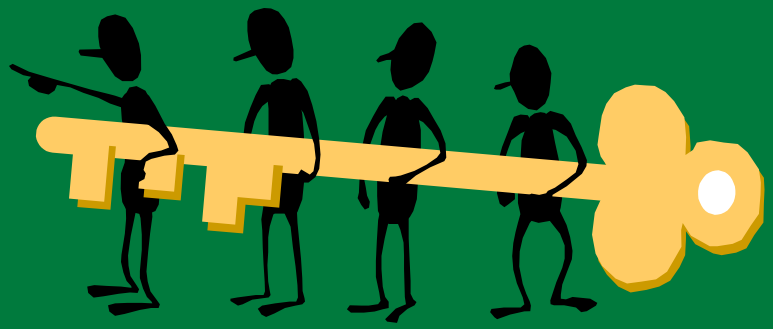
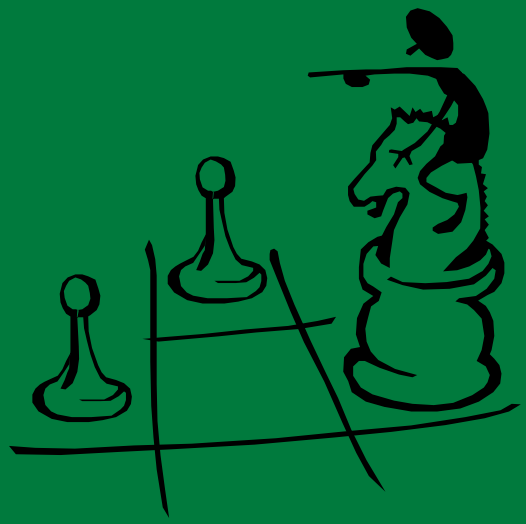
Five Keys to Successful Data-Driven Process Improvement

- #5: Create efficient cross-functional teams to drive and close-out investigation and improvement initiatives





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