

Morphine Extraction from Poppies

Lean Six Sigma Black Belt Project using JMP Statistical Discovery Software

David Payne
Head of Continuous Improvement

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Andrew Ruddick
Director
Process Insight Consulting



- Macfarlan Smith & Process Insight Consulting
- The Morphine supply chain
- Define the problem
- Collecting plant performance data
- Using JMP to analyse data sets
- Bring the process under control
- Future work using JMP



Process Insight

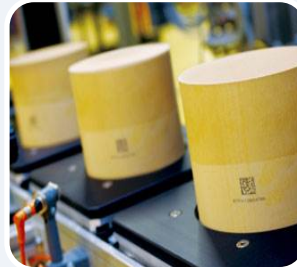
We help you maximise the value of your data by driving practical application of stats into the heart of your business

- Exploiting the power of JMP ® to solve your toughest real world problems
- Data Analytics for non – statisticians
 - “We speak human ! ”
- Engaging the total organisation in problem solving



Johnson Matthey

Johnson Matthey is a speciality chemicals company and a world leader in advanced materials technology.



Fine Chemicals

- API
Manufacture

- Catalysts &
Chiral
Technology

- Research
Chemicals

Emission Control Technologies

- Auto Catalysts

- Heavy Duty
Diesel

- Stationary
Emissions
Control

Precious Metal Products

- Refining,
recycling &
management

- Noble metals,
metal joining &
Colour
Technologies

Process Technologies

- Catalysts

- Davy
Technologies

- Tracerco

New Businesses

- Fuel Cells

- Battery
Technologies

- Water
Technologies

- New Business
development



- Manufacture Active Pharmaceutical Ingredients (APIs) for world wide supply

- Major products are alkaloids derived from the opium poppy (opiates) and synthetic opioids.



- World's largest supplier of opiate APIs with the widest product portfolio of opiate products for the pain relief market



- The largest consumer of “poppy” raw materials (morphine, thebaine and oripavine)

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The Supply Chain



Grow poppies
(UK & Portugal)



Harvest Poppies



Separate seed &
pelletise straw



Transfer in to plant
from containers

Project Scope



Solvent extract
Morphine in belt
extractor



Purify product, recover
solvent & isolate
Morphine as
"CPS" (concentrated
Poppy Straw)

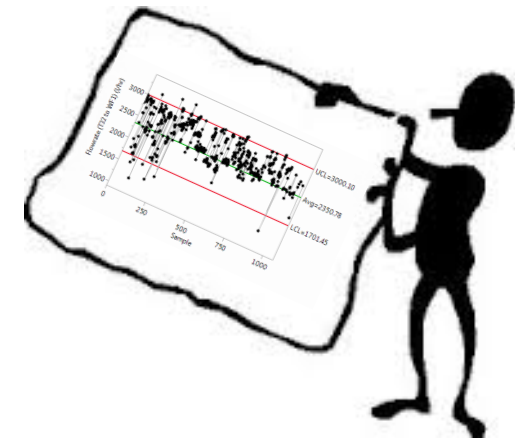


CPS is the raw
materials for the
manufacture of
many opiate
products

Codeine Phosphate
Codeine Sulphate
Codeine Alkaloid Pure
Dihydrocodeine

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- Big investment made but plant not delivering to target capacity
- Critical business need to increase output but process chaotic
 - Extremely difficult problem to solve!
- But solution will deliver huge value to the business



Poppy Growing



Out of Scope

Morphine Extraction



Purification & Solvent Recovery



In Scope

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Lots of Data to Collect & Analyse



Poppy Growing Data

- Field
- Variety
- Fertiliser
- Pesticide
- Drill date
- Harvest date
- Weed content
- Seed content
- Pelletising conditions
- Morphine content
- Sugars
- Starches



Extraction Plant Data

- Bulk density
- Morphine content
- Belt speed
- Gate Height
- Morphine rate
- Poppy straw rate
- Solvent rate
- Solvent ratio
- Recirculation rate
- pH
- Concentrations through the plant
- Flows through the plant
- Yield through the plant



Plant Performance Data

- Downtime hours
- Equipment breakdown
- Processing delays
- Technical delays
- Cleaning times
- Tar formation
- Filtration issues
- Percolation issues
- Separation issues

Data stored in lots of different systems which we can bring together in JMP and easily update using simple scripting



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Initial Plant Control Findings



Straw fed from silos to a
hopper above the
extractor



Operators can change extraction
conditions to satisfy various plant
targets



Solvent charged
to the belt to
extract the
Morphine

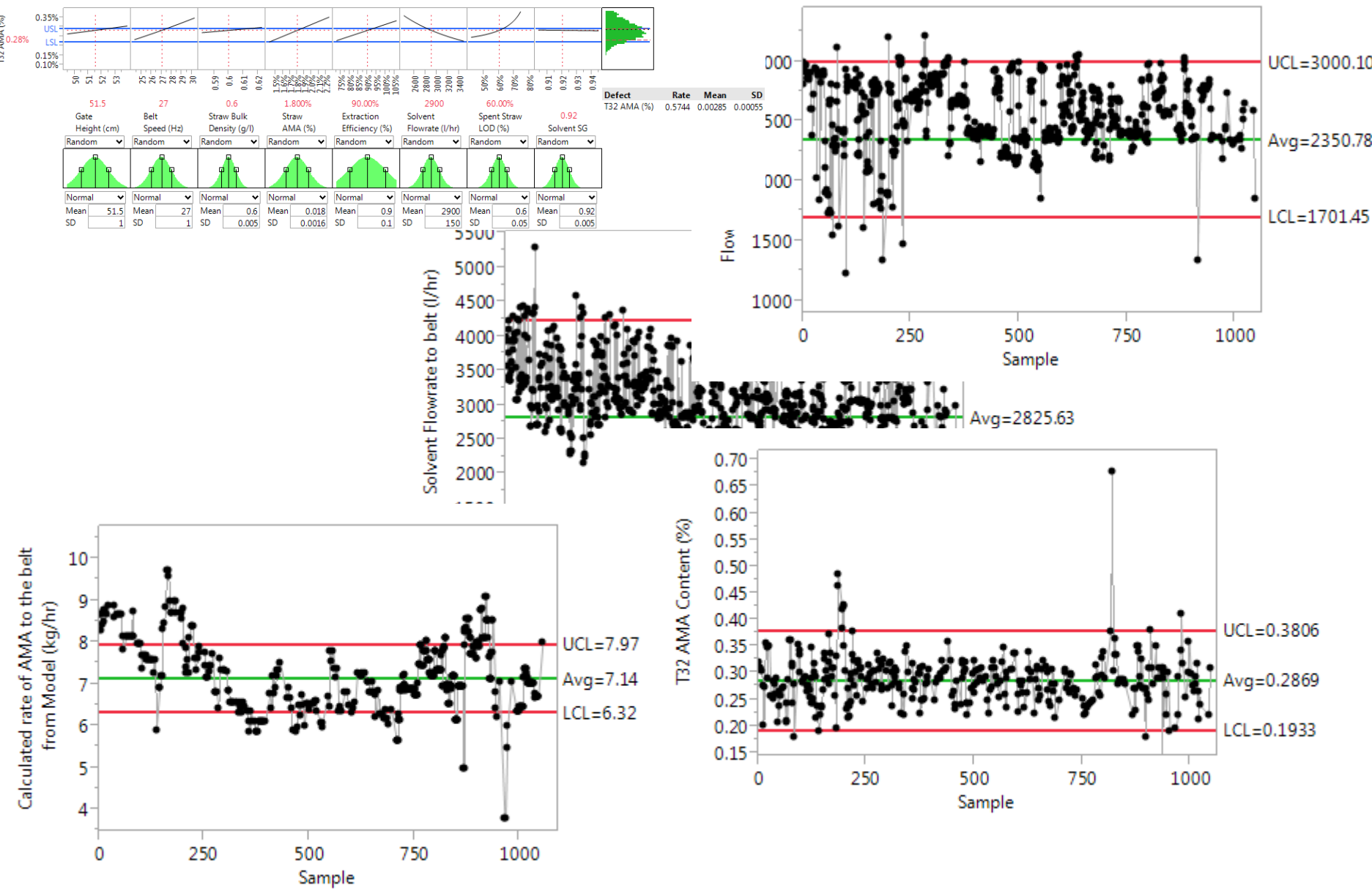


Rate to the extractor is
controlled by adjusting
belt speed and gate
height



**Target = 0.26%
Morphine post
extractor**

Link to JMP to show charts below



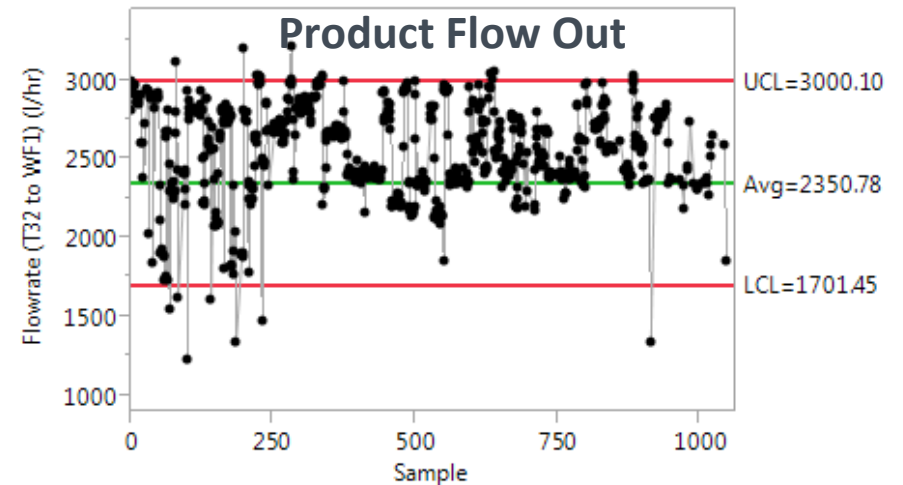
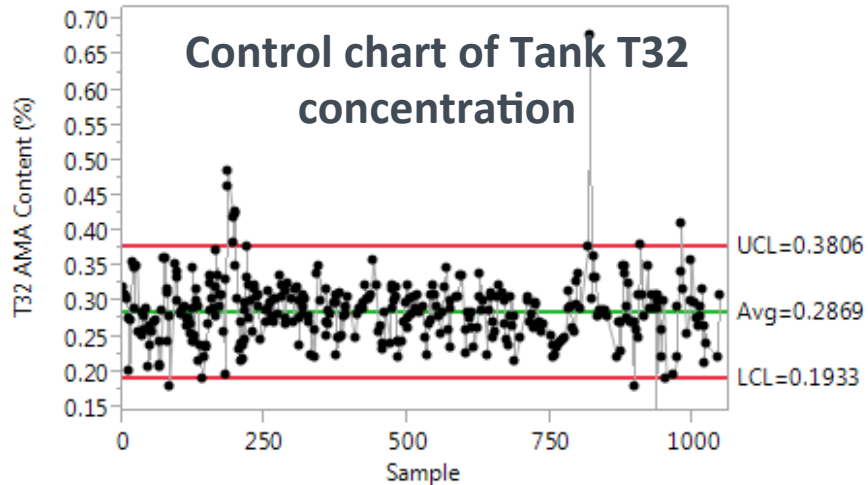
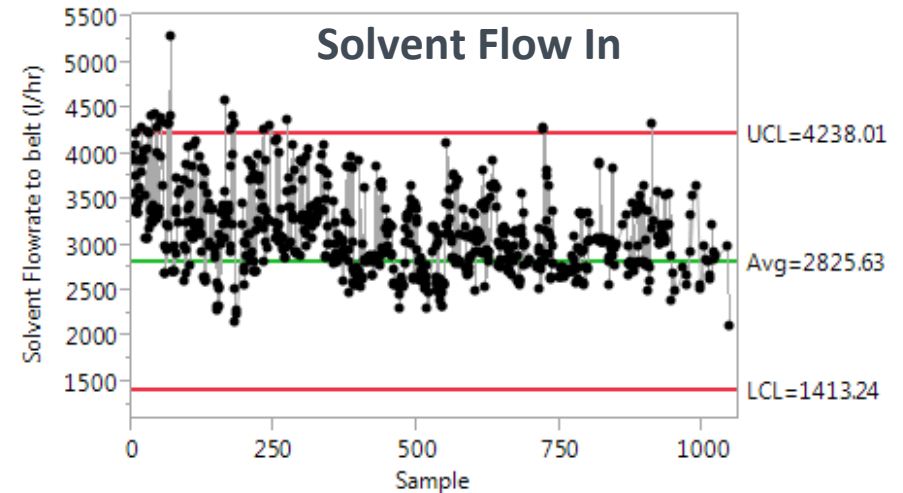
Implications of Poor Control

Morphine concentrations and flows to the purification stage are **not in control**:

Over concentrate – yield lost to waste stream and increased risk of choking plant

Under concentrate – under utilised equipment & lost capacity

Dilution Water Flowrate



- Morphine rate and Solvent feed into the plant are not well controlled



- Morphine concentrations and solvent flow from the extractor are highly variable and off target



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Split improvements into 3 stages:

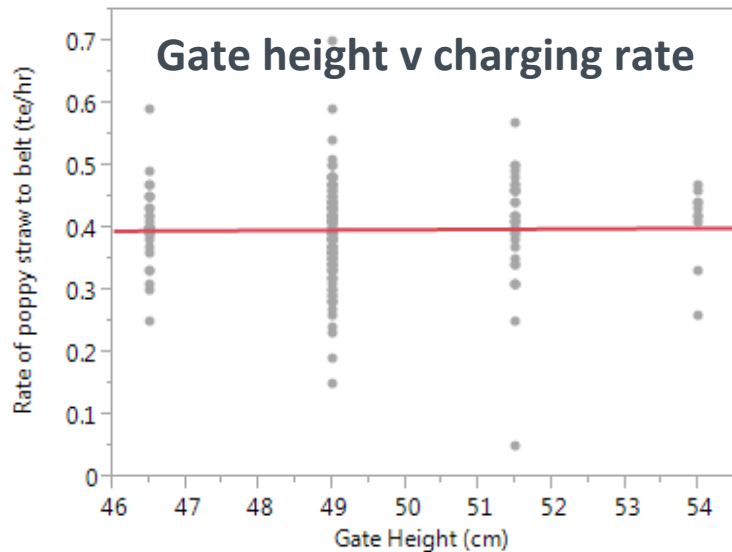
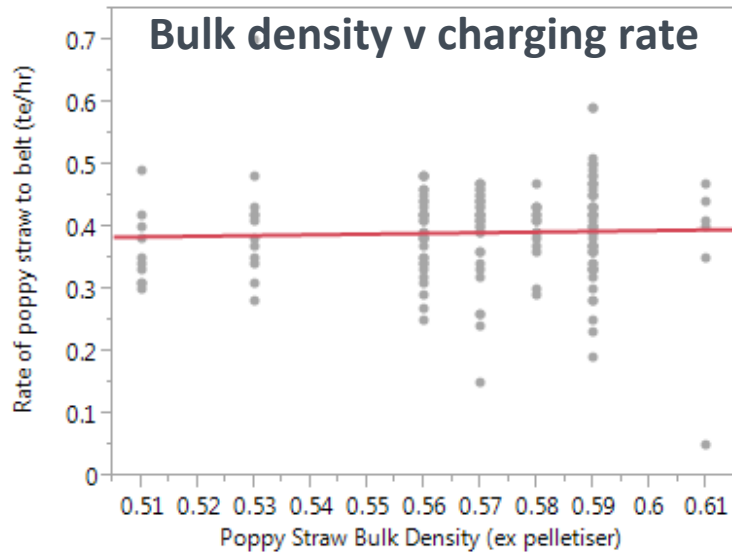
1. Control feeding rate and therefore Morphine into the plant
2. Demonstrate concentration & flow control
3. Optimise concentrations & flows to maximise output

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Initial Data Analysis Findings – Feed Rate

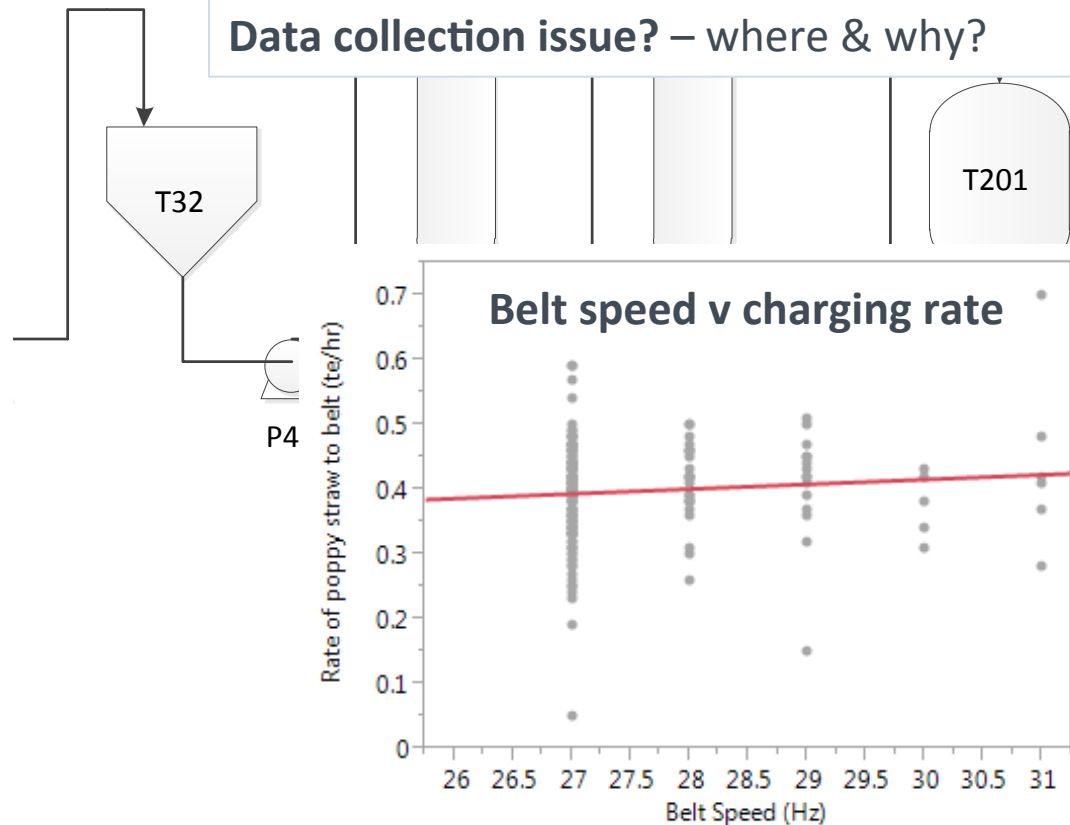
Dilution Water Flowrate



Parameters thought to control charging rate show no correlation:

Something else controlling it? – what?

Data collection issue? – where & why?



Initial Data Analysis Findings – Feed Rate

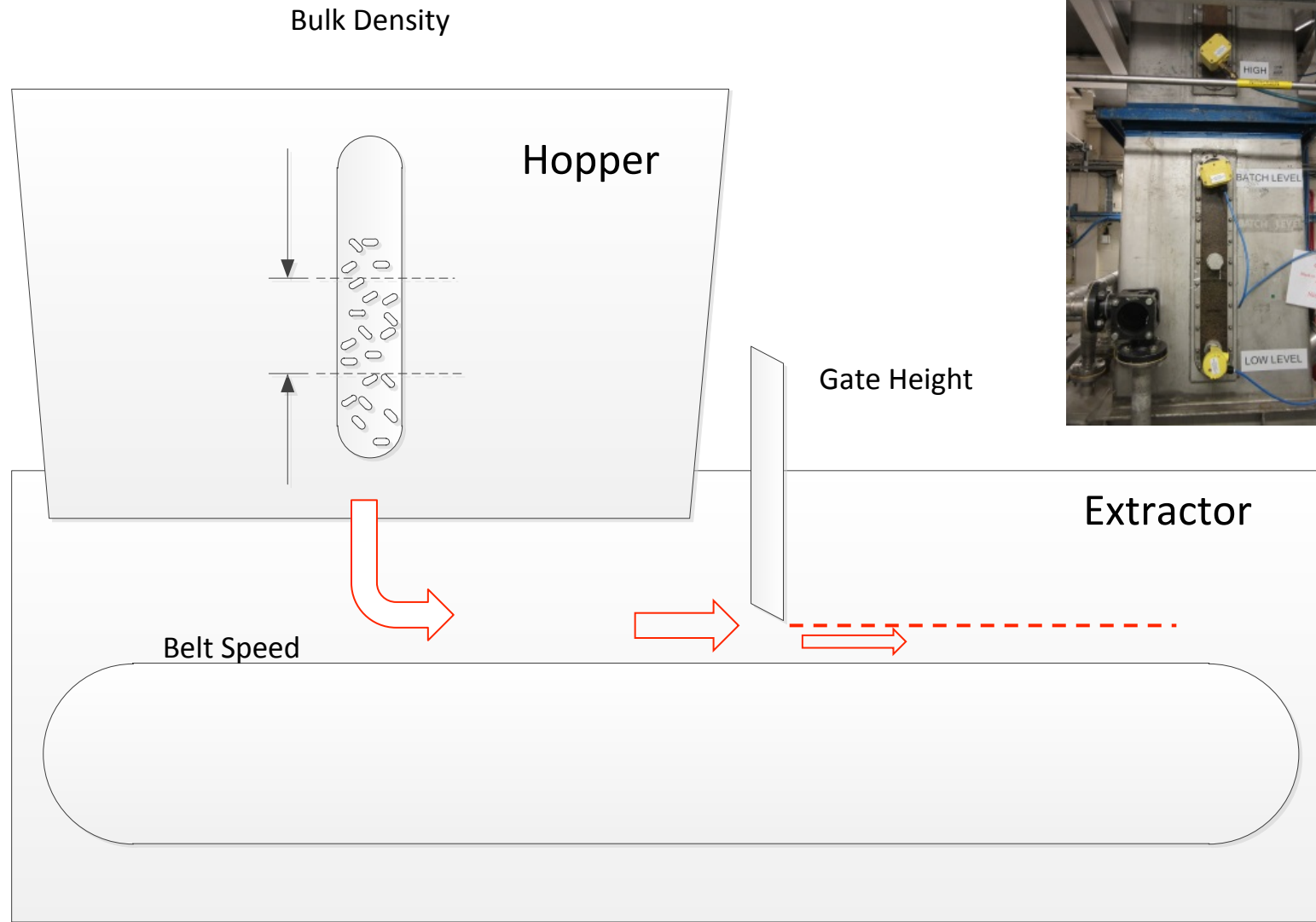


Conclusions:

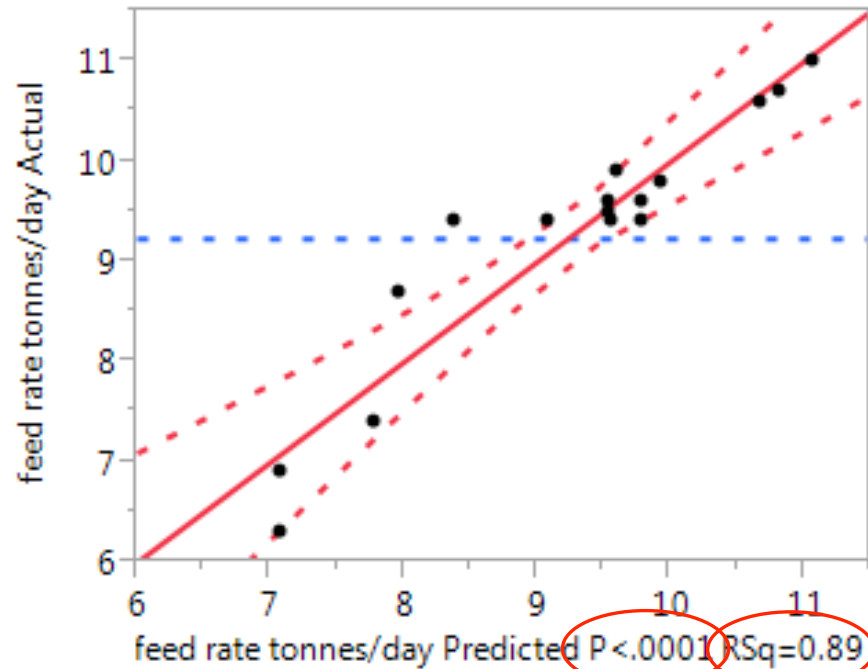
Existing method for calculating straw feed rate is flawed....

.....Needs a new approach

Improvement 1 – New Feed Rate Method



Improvement 1 - Feed Rate Model

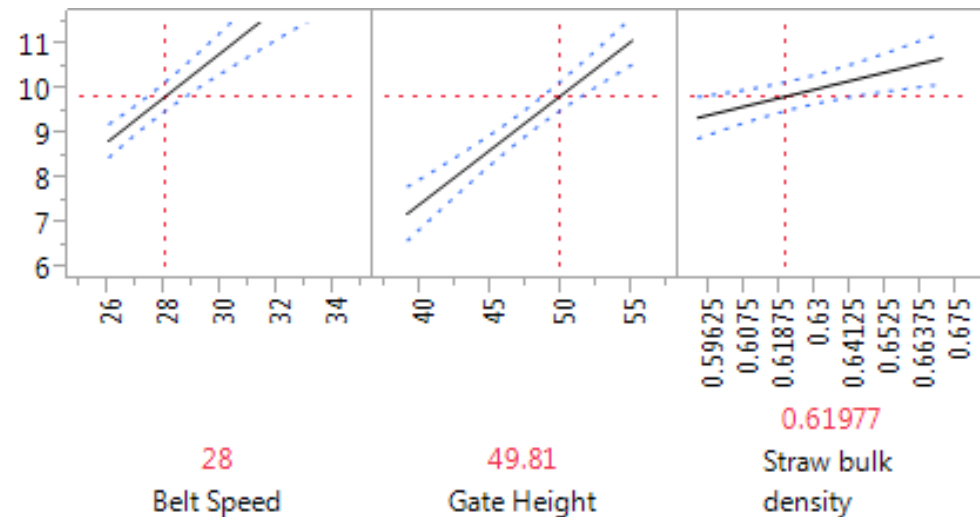


R Squared value shows how much of the variability the model explains – nearly 90%

P value indicates model is statistically significant

feed rate tonnes/day
9.853719
[9.528974, 10.17846]

Prediction Profiler in JMP



Split improvements into 3 stages:

1. Control feeding rate and therefore Morphine into the plant **Complete**
2. Demonstrate concentration & flow control
3. Optimise concentrations & flows to maximise output

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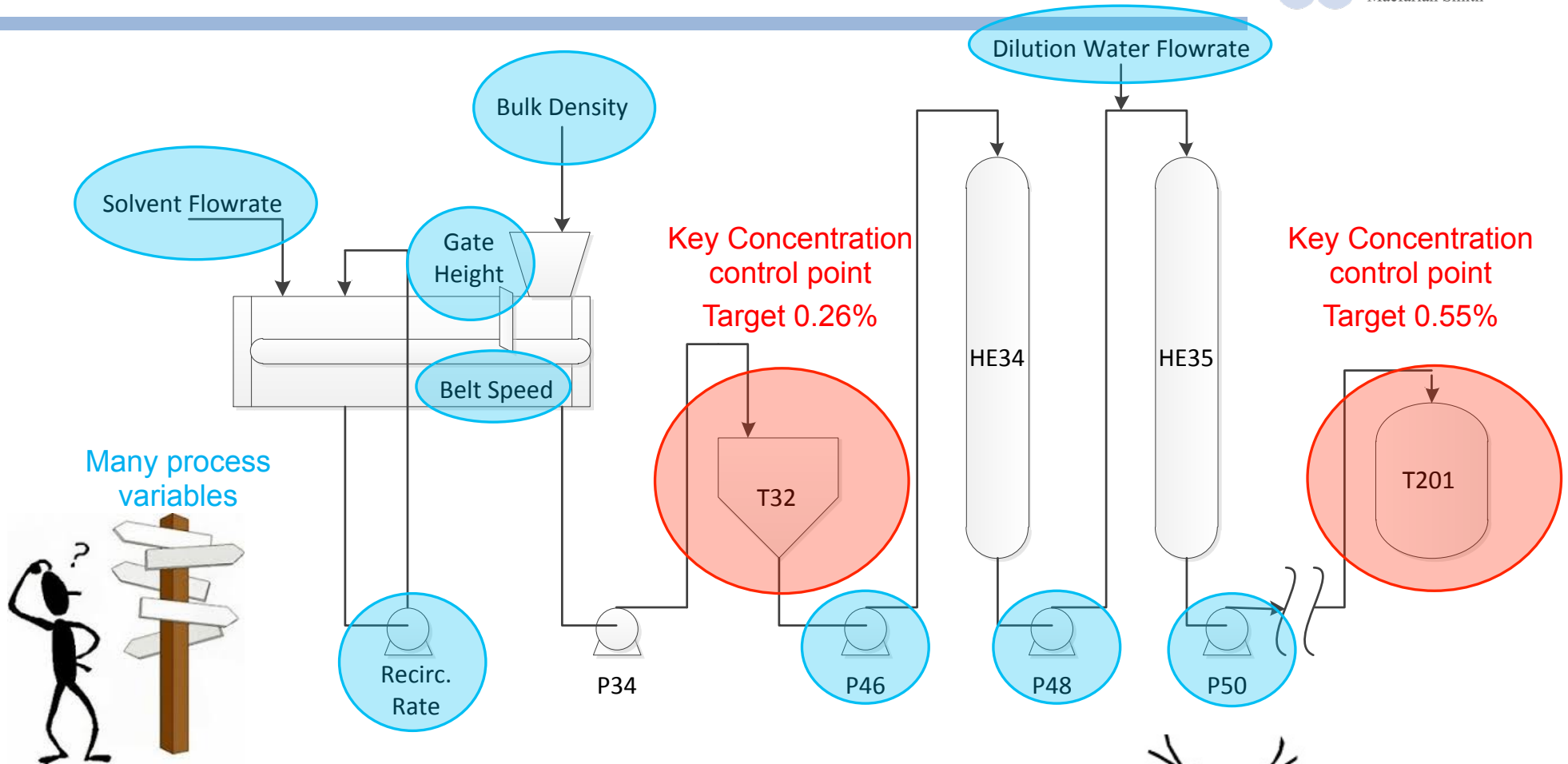
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Complete

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Current Concentration Control Method

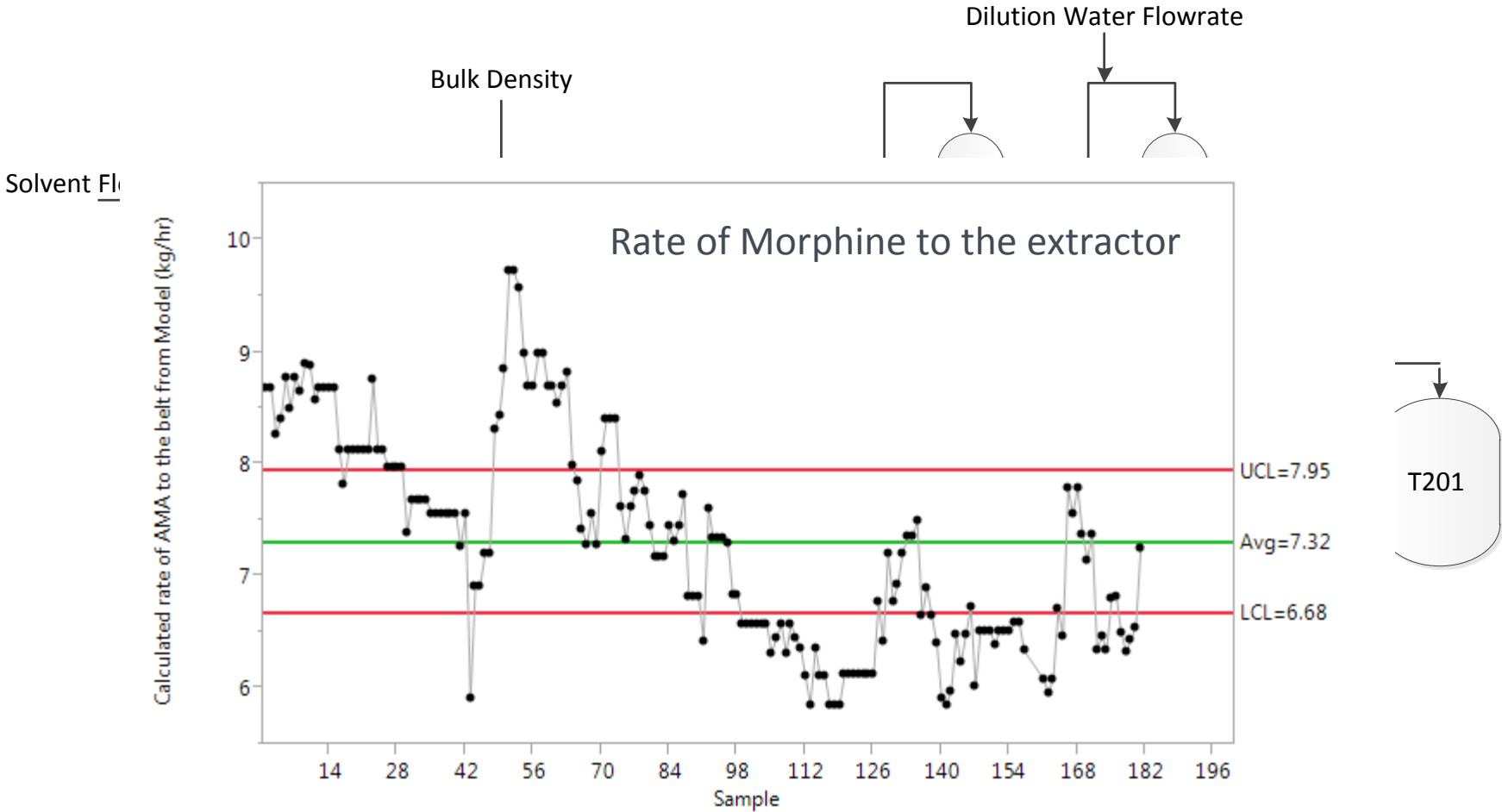


- Multiple key concentration control points
- Many critical process variables
- Continuous processing plant with lots of interactions
- No understanding of the effect one change has on another

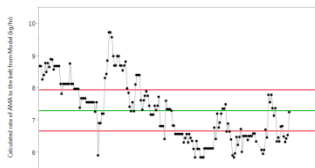


JMP

Improvement 2 - Current Control Method



Improvement 2 - Current Control Method

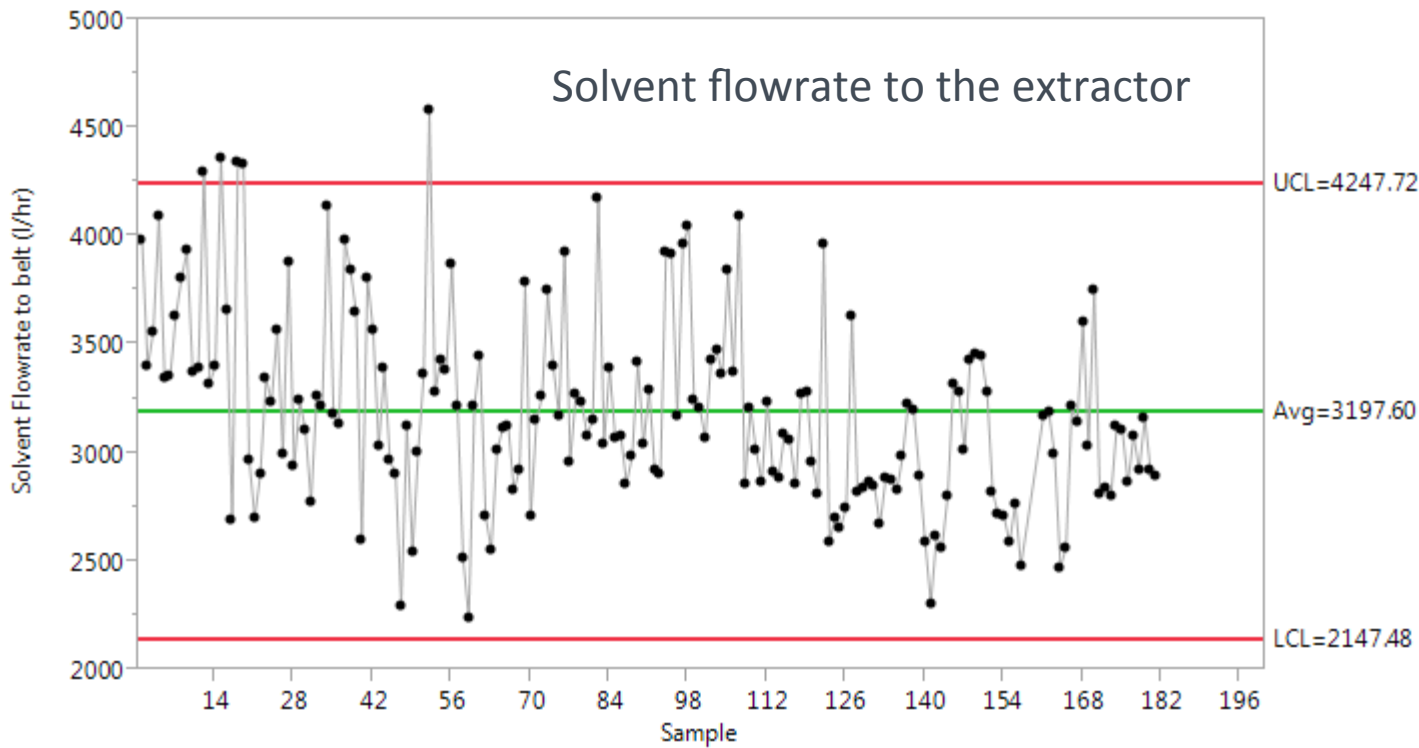


Bulk Density

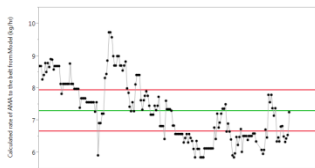
Dilution Water Flowrate



Solvent Flowrate



Improvement 2 - Current Control Method

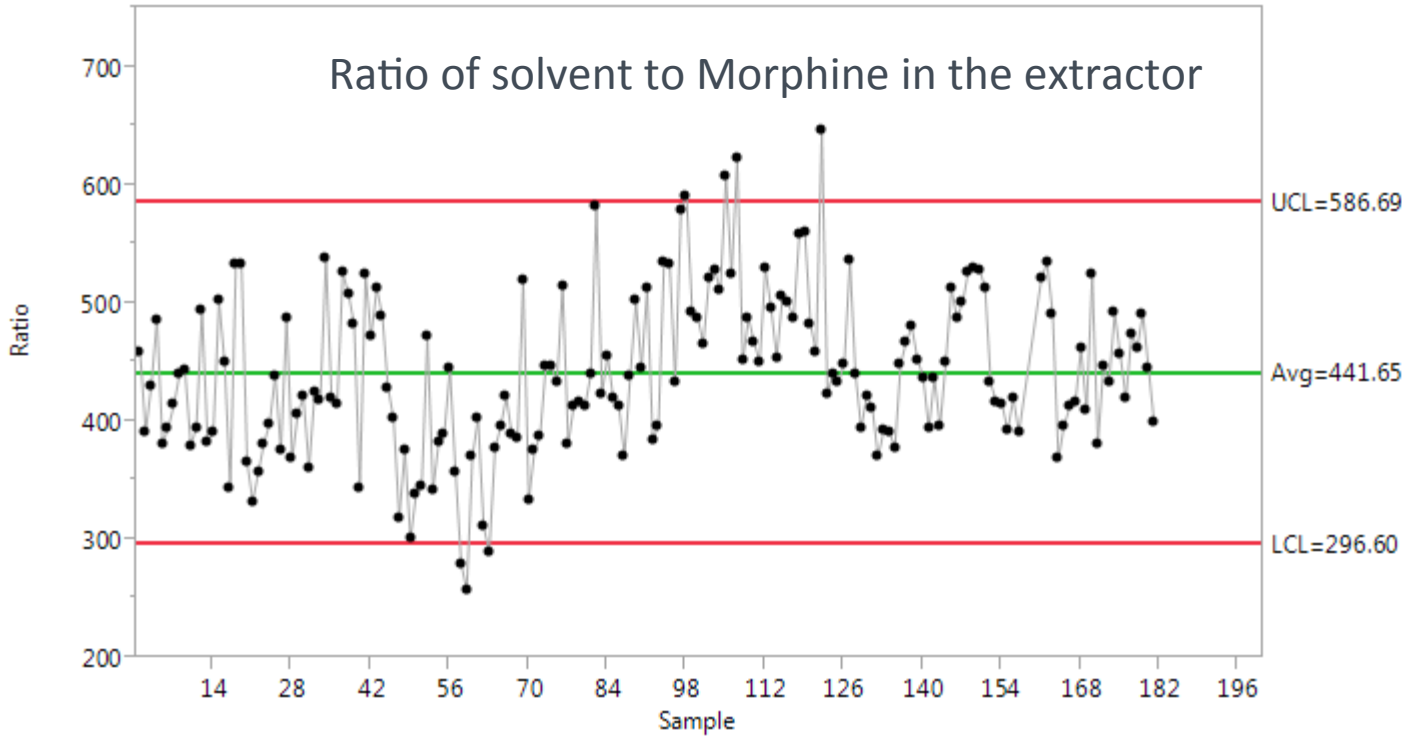
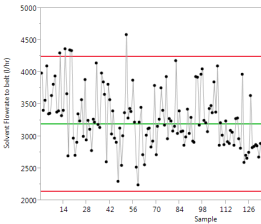


Bulk Density

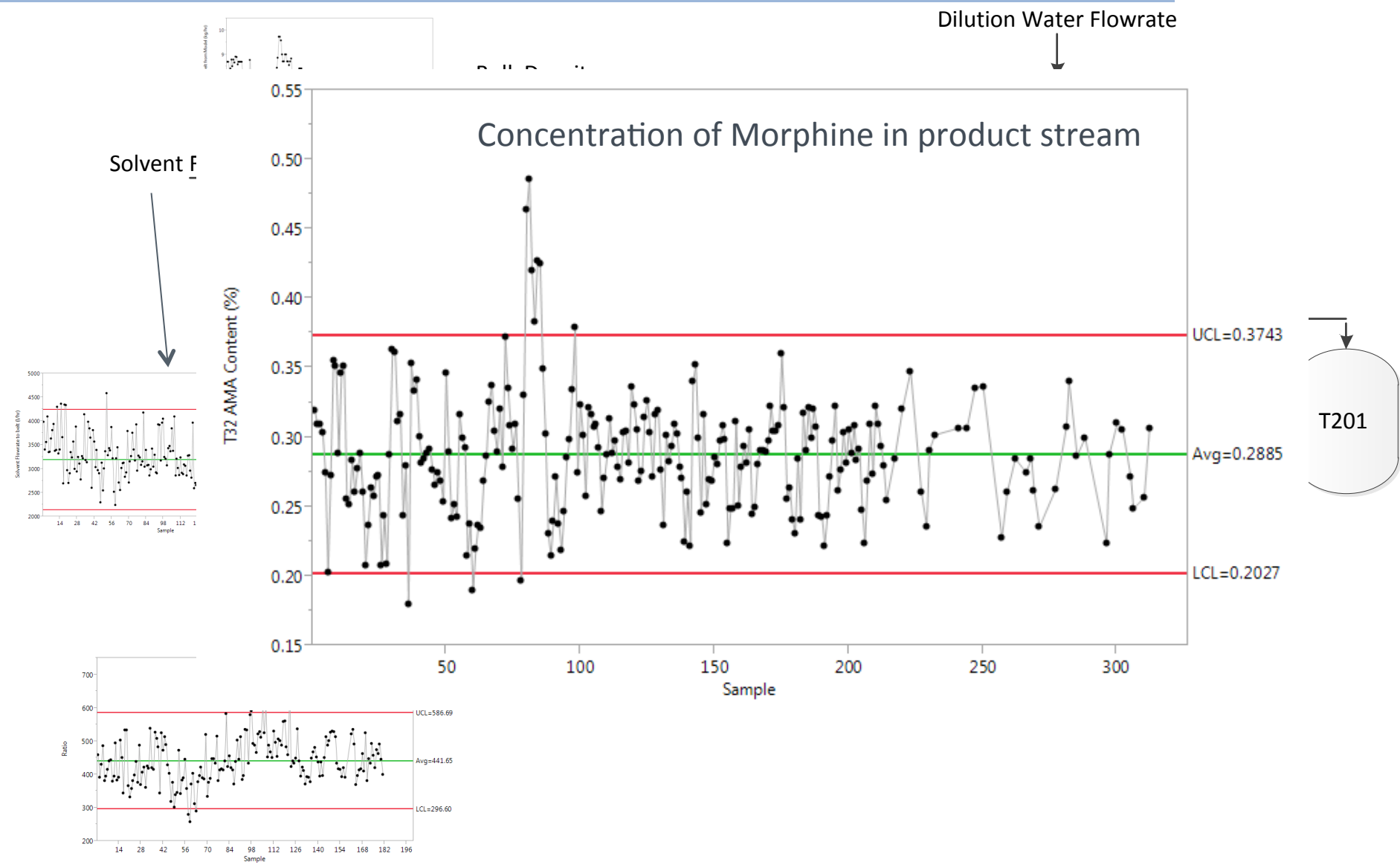
Dilution Water Flowrate



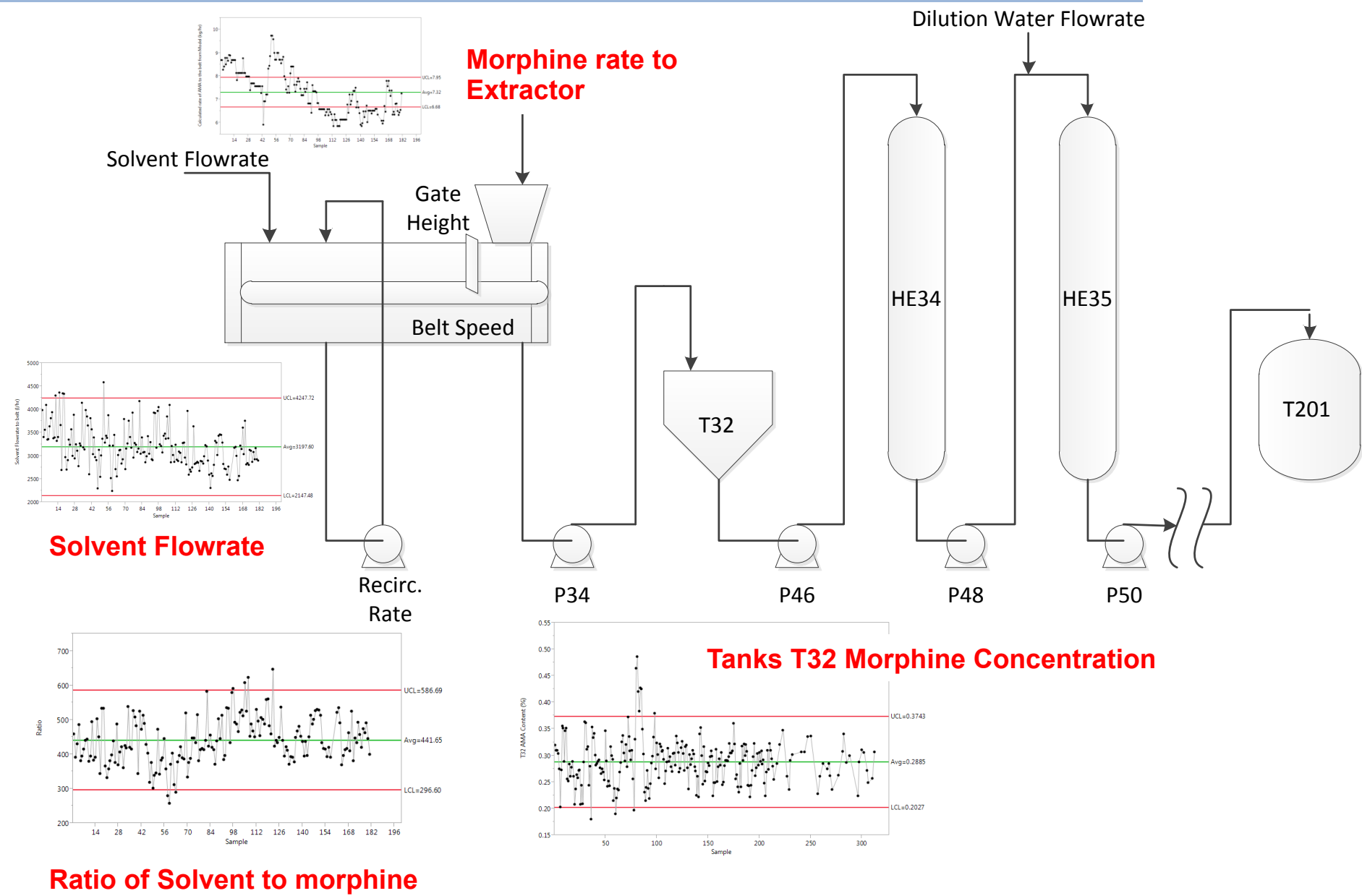
Solvent FI



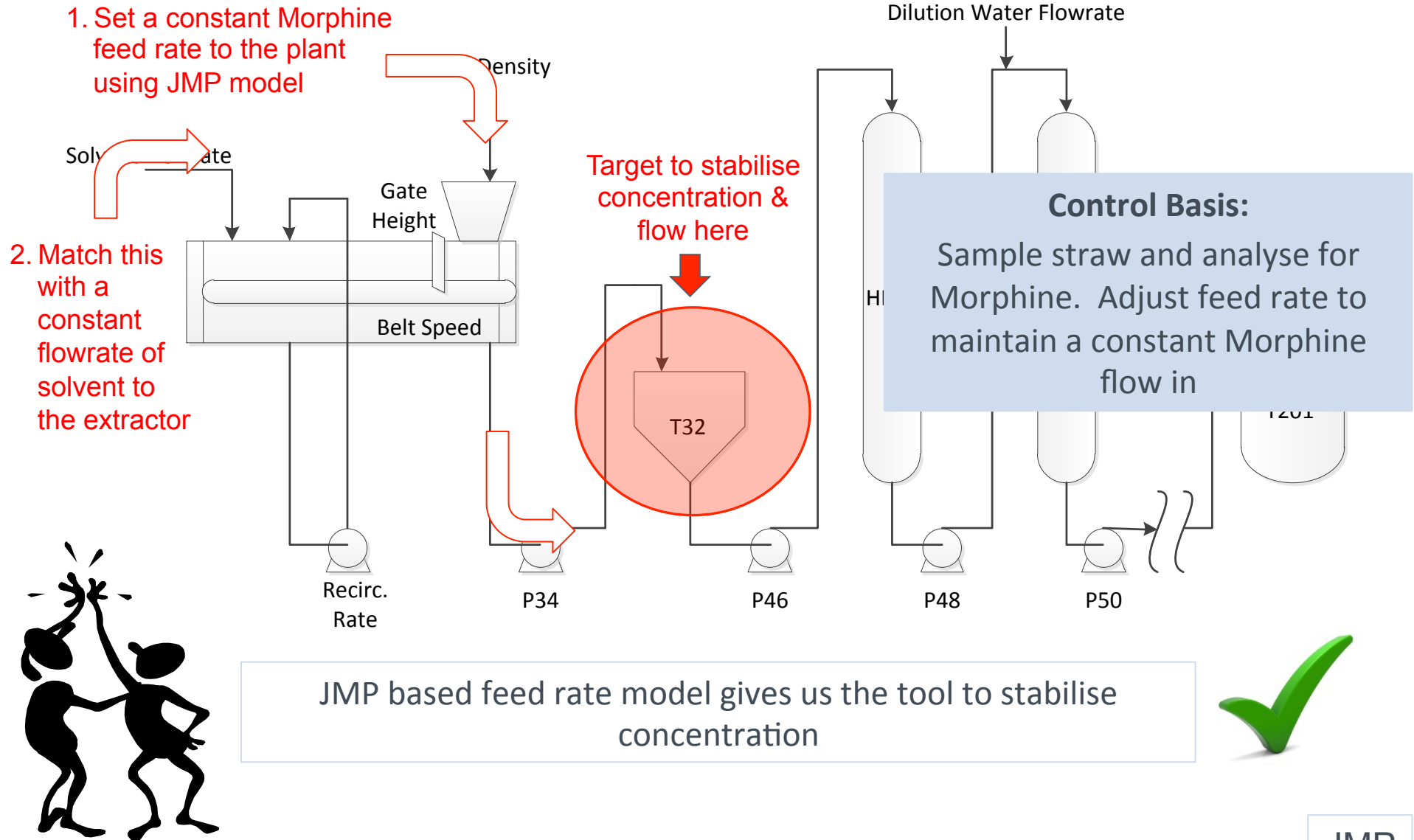
Improvement 2 - Current Control Method



Current Control Method

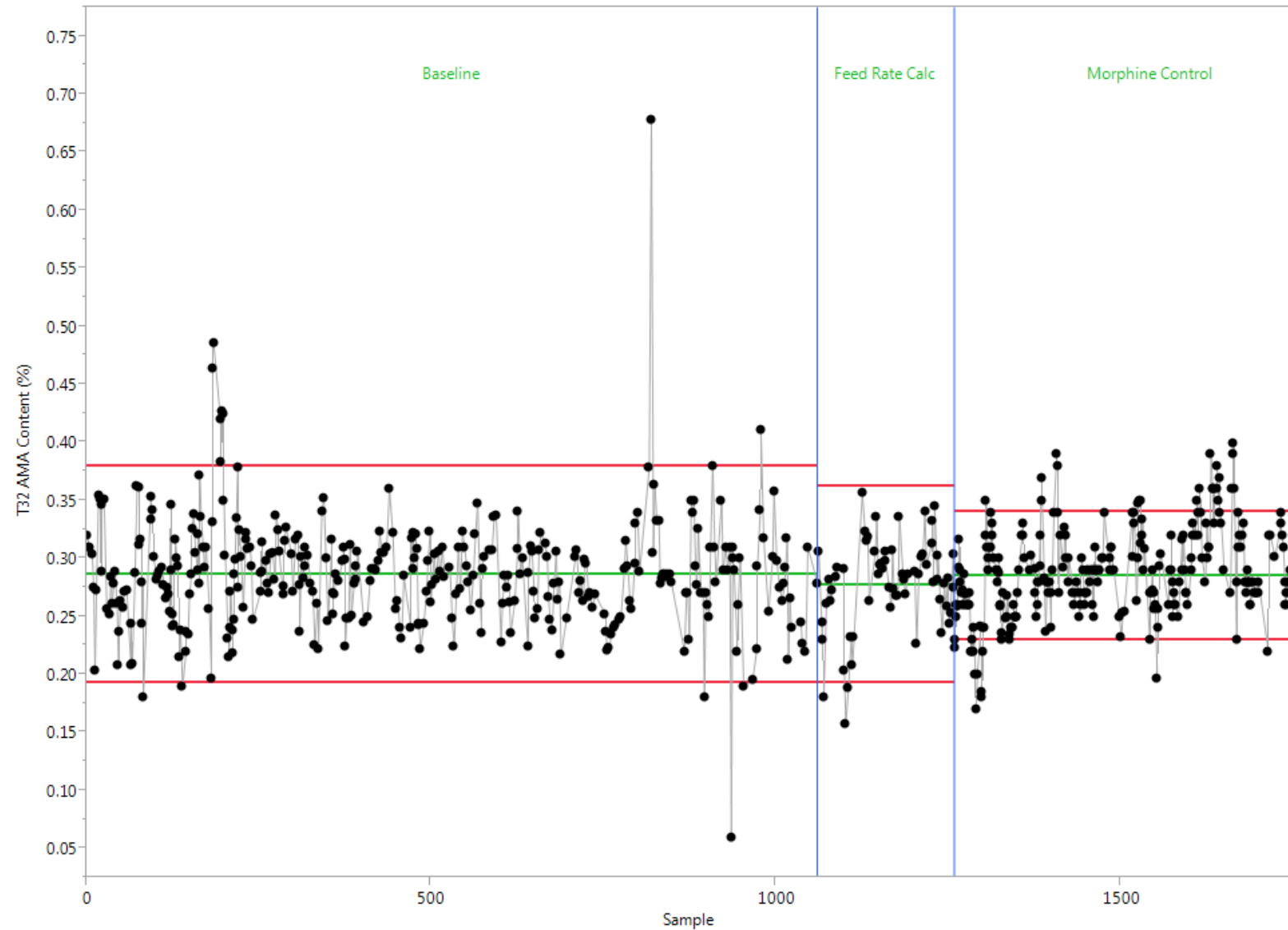


Improvement 2a – Morphine Control Method



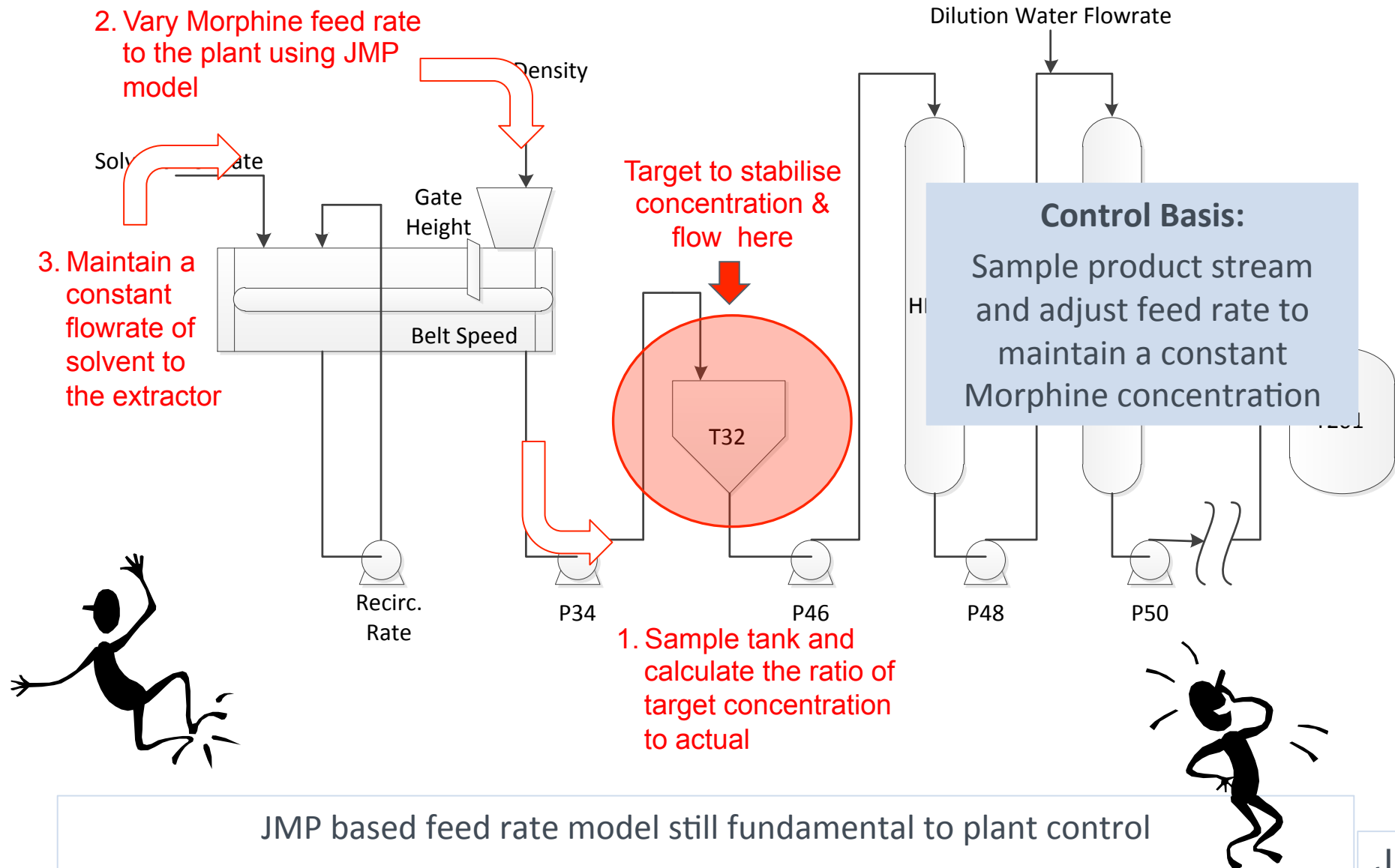
JMP

Improvement Result for Morphine Control

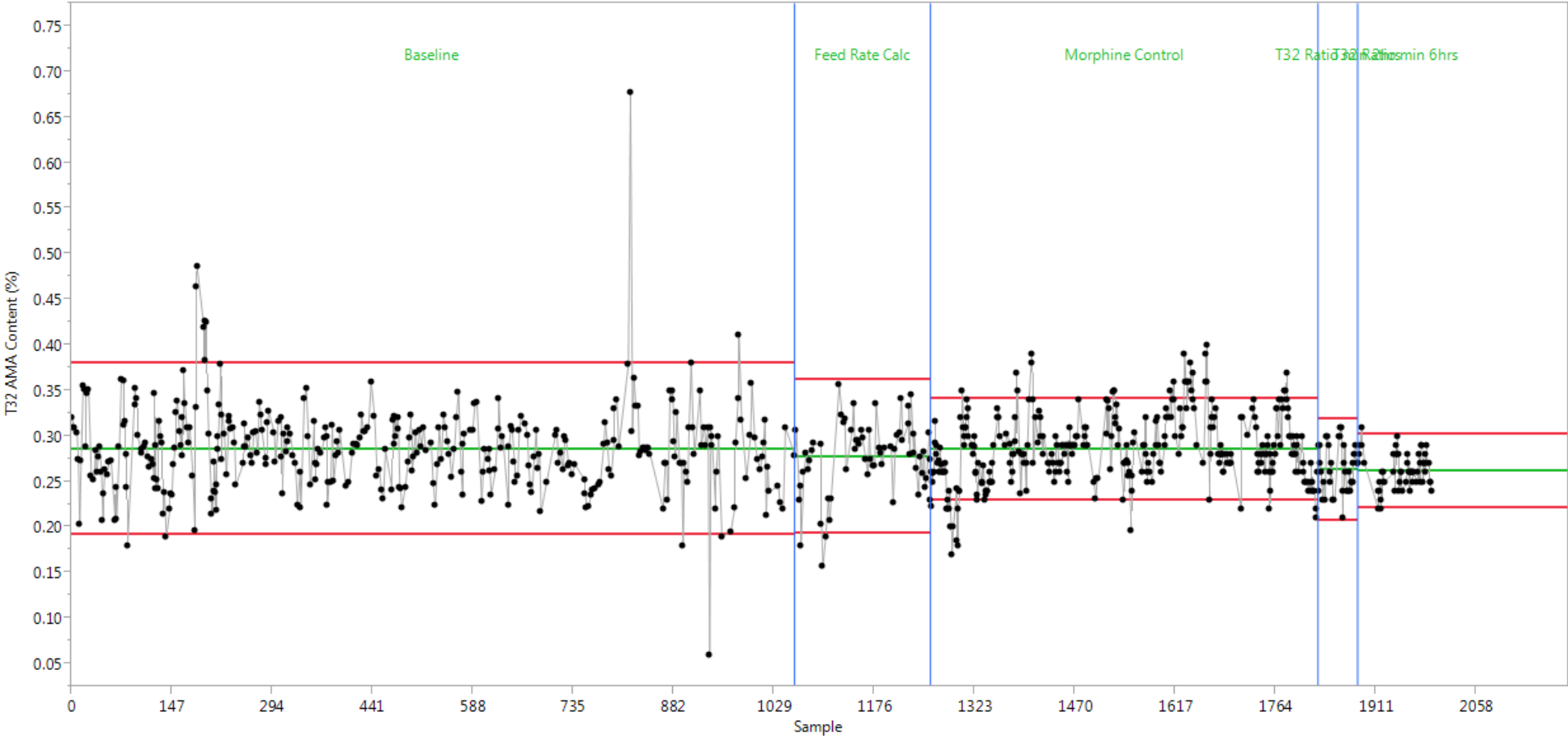


Prediction Profiler

Improvement 2b – Ratio Control Method



Improvement Results in JMP



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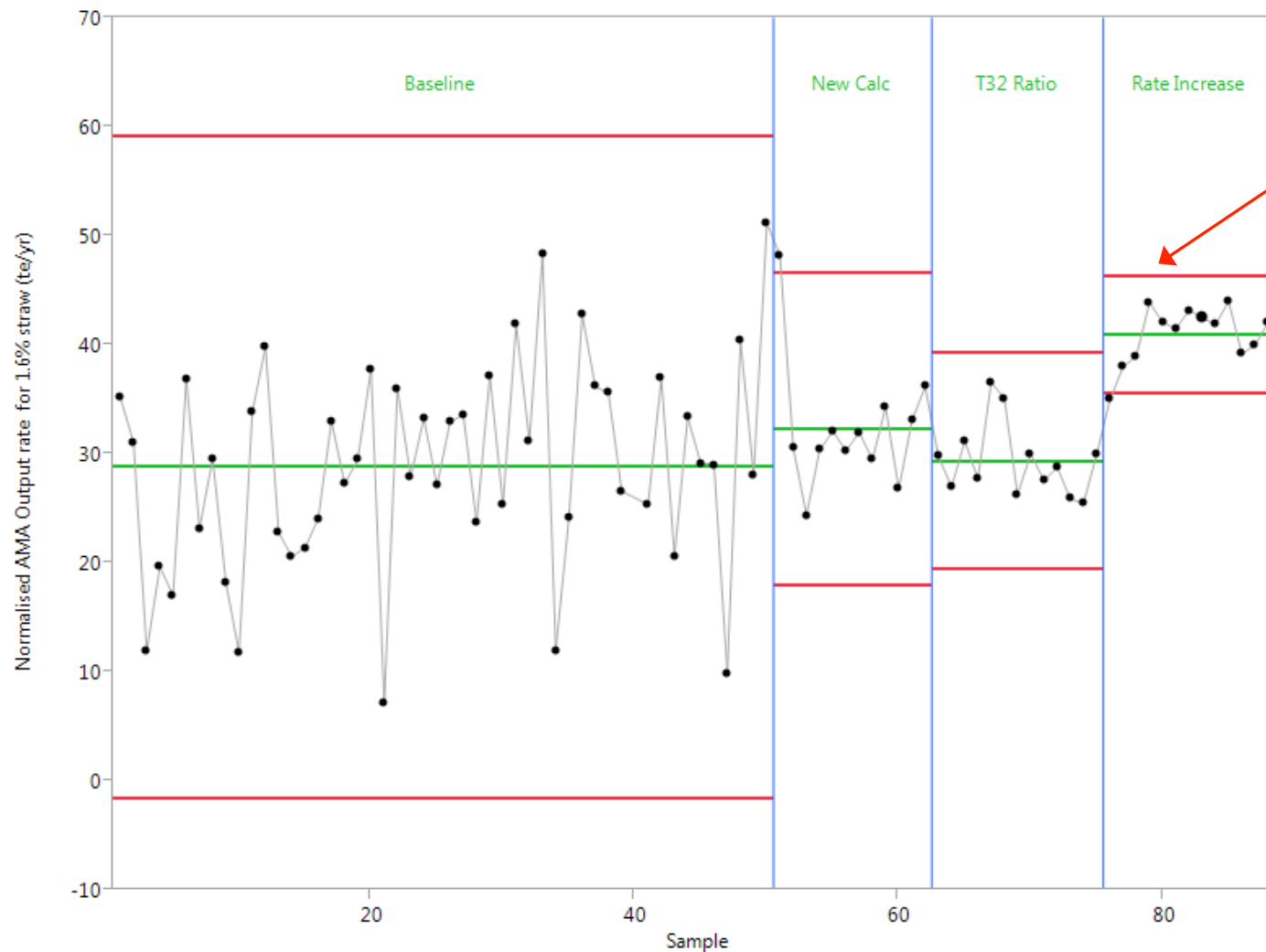
Complete

2. Demonstrate concentration & flow control

Complete

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Improvement Results

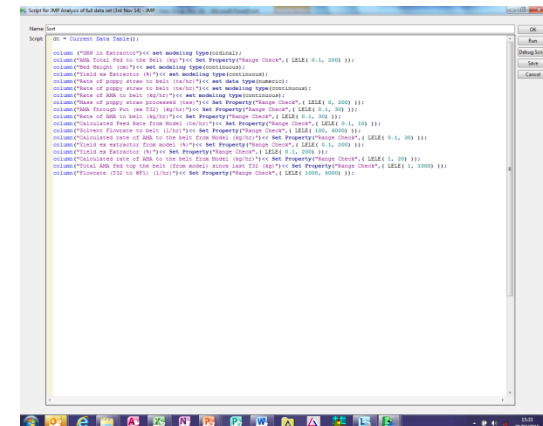
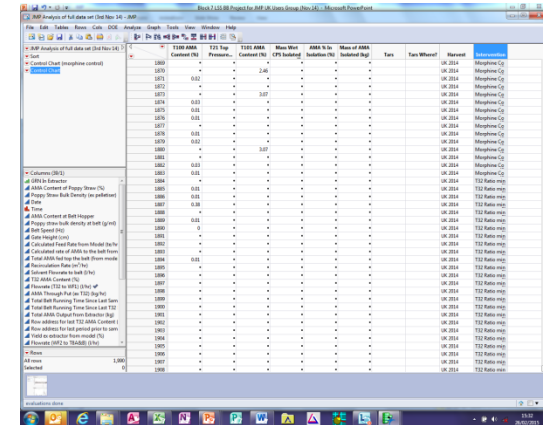
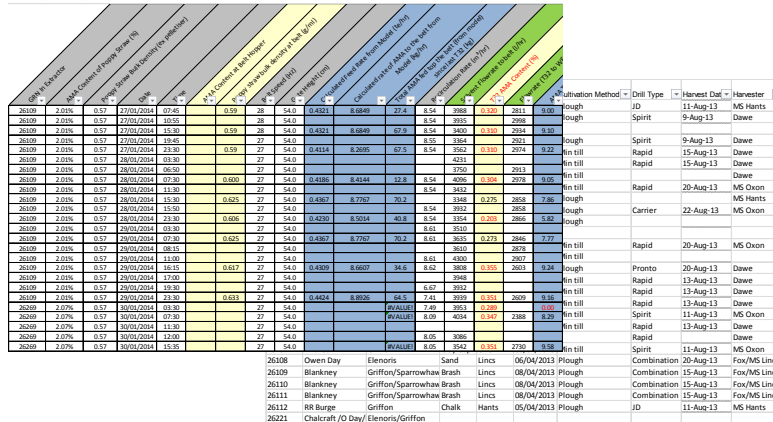


Rate increased incrementally over several weeks all the time using JMP to analyse data and ensure key parameters remained in control

**CONTINUOUS
IMPROVEMENT**
Macfarlan Smith



JMP Script to create dashboard



Split improvements into 3 stages:

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Complete

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Complete

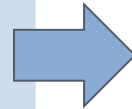
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Next Steps – Vertical Integration of CI work



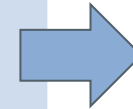
Poppy Growing Optimisation

- Growing locations
- Growing conditions
- Poppy variety
- Fertilizer type
- Pesticide type
- Drill dates
- Harvesting point
- Pellet type
- Reduced product variability



Extraction Optimisation

- Extraction conditions
- Purification conditions
- Morphine product specification



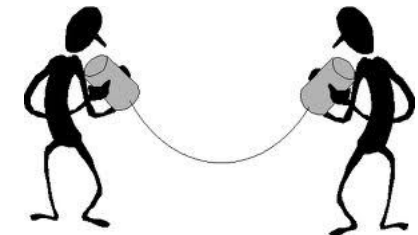
Opiate Processes Optimisation

- Process conditions to maximise yield
- Process conditions to minimise impurities
- Minimise process variability
- Increase product RFT rate



We Could Not Have Done This Without JMP

- Pin point the issues in a fog of data
- Visualise the data to easily spot patterns, trends & outliers
- Powerful modelling, profiling & what-if simulation
- Easy communication of process issues through simple visualisation
- Ease of data clean up, manipulation & dash-boarding





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IMPROVEMENT**
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