ISPE Carolina-South Atlantic Chapter

Lean Manufacturing & Energy Management Projects at Morrisville Facility

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Merck Biomanufacturing Network

- RTP Facility is part of the Merck's BioManufacturing Network in conjunction with a biomanufacturing facility in Bilingham, England
- In November 2009, Merck completed its merger with Schering-Plough Corporation
- Third Party Biopharmaceutical Contract Manufacturing
- Manufacturing of Active Pharmaceutical Ingredients (API)
  - Commercial
  - Clinical

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Merck Rationale

Diosynth™ BIOTECHNOLOGY + MSD

Formerly Avecia Biologics

- Exists as a top tier CMO now
- Retains and builds technical excellence across a range of biologics

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Programs offered by Diosynth

- Program 1: Process Development
  - Fermentation
  - Purification
  - Analytical Development
- Program 2: Scale-up and Clinical Manufacture
  - Tech Transfer
  - Engineering run(s)
  - cGMP Manufacture to support Phase III
- Program 3: Process Validation
  - Laboratory process characterization
  - Analytical method validation
  - Engineering run
  - Process Validation runs
- Program 4: Commercial Manufacture

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Lean Manufacturing at Diosynth

- Integrated Production Team (IPT) Structure
  - Fermentation
  - Cell Culture
  - Centers of Excellence (CoE)
- Number of current MPS Projects
  - >20 Projects
- # Kaizen executed
  - ~15 Kaizen's
  - Target of 2 per month

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Merck's Stance on Energy

- Merck believes that reducing our environmental impact is consistent with our values as a health care company
- The 2010 ENERGY STAR Sustained Excellence Award
- Merck, has been an ENERGY STAR partner since 2004
- Recognized by the EPA for five consecutive years
- Merck is committed to energy conservation and our vision to be the most efficient energy steward in the Pharmaceutical Industry

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What is motivating the Pharmaceutical industry to improve energy efficiency?

- Cost Reduction
- Energy/Utility Use Reduction
- Increasing cost & global volatility of energy supply
- Environmental responsibility and sustainability
- Greenhouse Gas Reduction
  - 10% reduction in GHG emissions based on 2008 baseline

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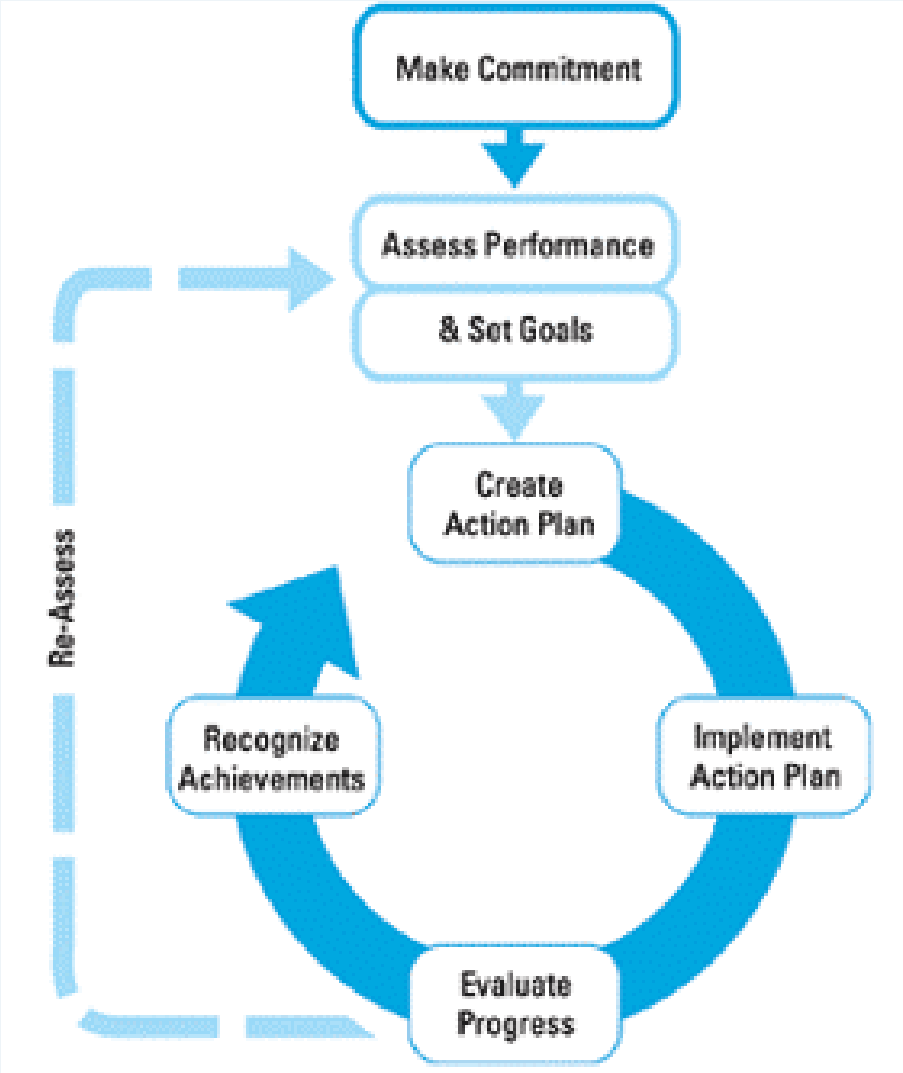
Guidelines for Energy Management Overview



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Self Assessment

ENERGY STAR® Energy Management Assessment Matrix

	Little or no evidence	Some elements	Fully implemented	Next Steps
Make Commitment to Continuous Improvement				
Energy Director	No central or organizational resource. Decentralized management	Central or organizational resource not empowered	Empowered central or organizational leader with senior management support	
Energy Team	No company energy network	Informal organization	Active cross-functional team guiding energy program	
Energy Policy	No formal policy	Referenced in environmental or other policies	Formal stand-alone EE policy endorsed by senior mgmt.	
Assess Performance and Opportunities				
Gather and Track Data	Little metering/no tracking	Local or partial metering/tracking/reporting	All facilities report for central consolidation/analysis	
Normalize	Not addressed	Some unit measures or weather adjustments	All meaningful adjustments for organizational analysis	
Establish baselines	No baselines	Various facility-established	Standardized organizational base year and metric established	
Benchmark	Not addressed or only same site	Some internal comparisons among	Regular internal & external comparisons	
Create Action Plan				
Define technical steps and targets	Not addressed	Facility-level consideration as opportunities occur	Detailed multi-level targets with timelines to close gaps	
Determine roles and resources	Not addressed or done on ad hoc basis	Informal interested person competes for funding	Internal/external roles defined & funding identified	
Implement Action Plan				
Create a communication plan	Not addressed	Tools targeted for some groups used occasionally	All stakeholders are addressed on regular basis	
Raise awareness	No promotion of energy efficiency	Periodic references to energy initiatives	All levels of organization support energy goals	
Build capacity	Indirect training only	Some training for key individuals	Broad training/certification in technology & best practices	
Motivate	No or occasional contact with energy users and staff	Threats for non-performance or periodic reminders	Recognition, financial & performance incentives	
Track and monitor	No system for monitoring progress	Annual reviews by facilities	Regular reviews & updates of centralized system	
Evaluate Progress				
Measure results	No reviews	Historical comparisons	Compare usage & costs vs. goals, plans, competitors	
Review action plan	No reviews	Informal check on progress	Revise plan based on results, feedback & business factors	
Recognize Achievements				
Provide internal recognition	Not addressed	Identify successful projects	Acknowledge contributions of individuals, teams, facilities	
Get external recognition	Not sought	Incidental or vendor acknowledgement	Government/third party highlighting achievements	

Make a Commitment

- Commit to Continuous Improvement
  - Changing the Culture
- Appoint an Energy Champion
- Create an Energy Team
- Start putting together Energy Policies

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Assess Performance

- Identify Savings Potential by Benchmarking
- Pharmaceutical Manufacturing Plant Energy Performance Indicator
  - US EPA's ENERGY STAR partnered with pharmaceutical companies to improve energy efficiency
  - EPA helps industry overcome barriers to using energy efficiently and provides energy management resources
  - Merck has 3 manufacturing plants that are ENERGY STAR certified
- http://www.energystar.gov/

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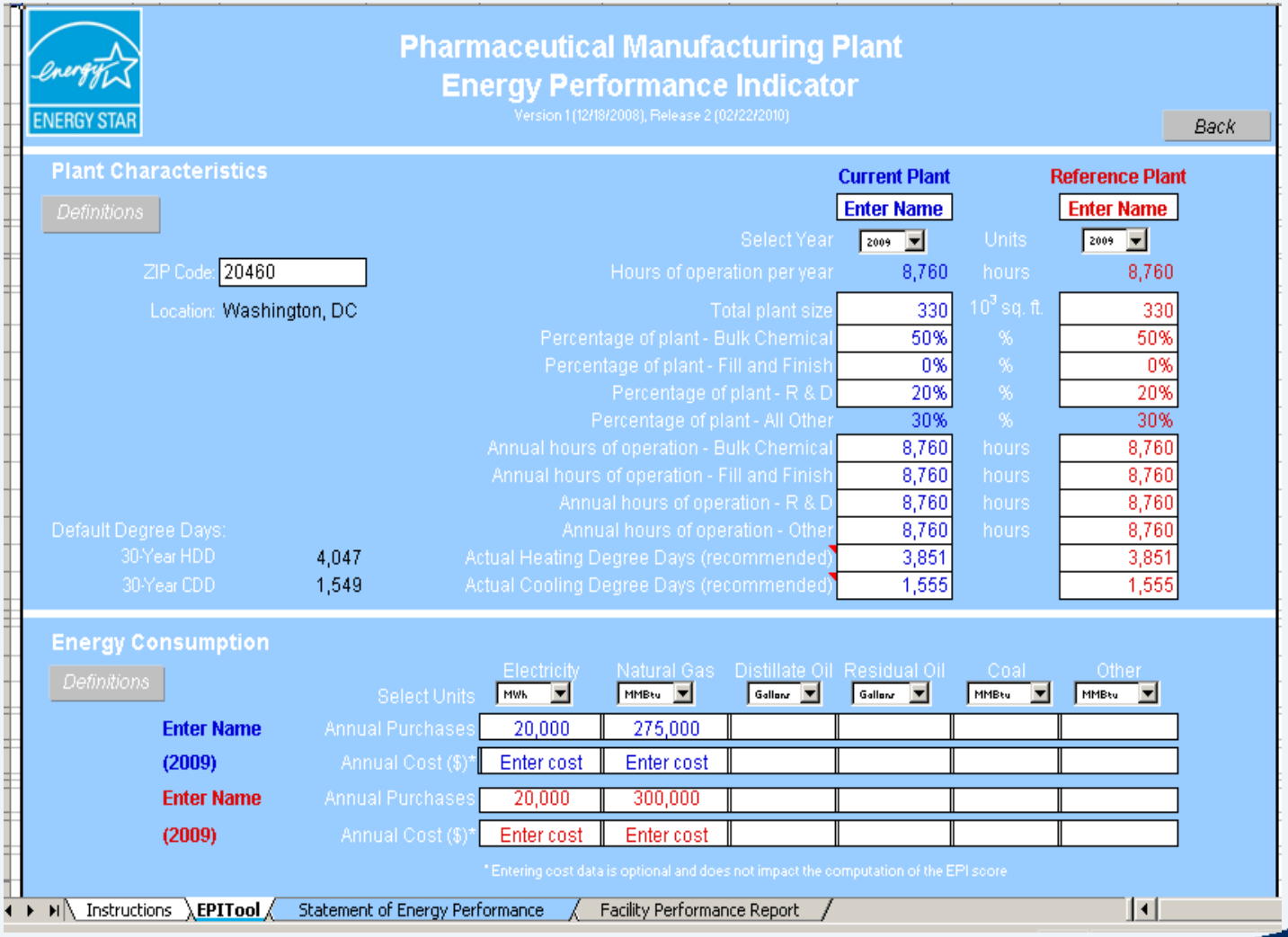
Benchmarking Tools



Pharmaceutical Manufacturing Plant
Energy Performance Indicator

Version 1 (12/18/2008), Release 2 (02/22/2010)

Back

Plant Characteristics

Definitions

ZIP Code: 20460

Location: Washington, DC

Default Degree Days:

30-Year HDD 4,047

30-Year CDD 1,549

	Current Plant: Enter Name	Units	Reference Plant: Enter Name
Select Year	2009		2009
Hours of operation per year	8,760	hours	8,760
Total plant size	330	10^3 sq. ft.	330
Percentage of plant - Bulk Chemical	50%	%	50%
Percentage of plant - Fill and Finish	0%	%	0%
Percentage of plant - R & D	20%	%	20%
Percentage of plant - All Other	30%	%	30%
Annual hours of operation - Bulk Chemical	8,760	hours	8,760
Annual hours of operation - Fill and Finish	8,760	hours	8,760
Annual hours of operation - R & D	8,760	hours	8,760
Annual hours of operation - Other	8,760	hours	8,760
Actual Heating Degree Days (recommended)	3,851		3,851
Actual Cooling Degree Days (recommended)	1,555		1,555

Energy Consumption

Definitions

		Electricity	Natural Gas	Distillate Oil	Residual Oil	Coal	Other
	Select Units	MWh	MMBtu	Gallons	Gallons	MMBtu	MMBtu
Enter Name (2009)	Annual Purchases	20,000	275,000				
	Annual Cost ($)*	Enter cost	Enter cost				
Enter Name (2009)	Annual Purchases	20,000	300,000				
	Annual Cost ($)*	Enter cost	Enter cost				

* Entering cost data is optional and does not impact the computation of the EPI score

Instructions | EPITool | Statement of Energy Performance | Facility Performance Report

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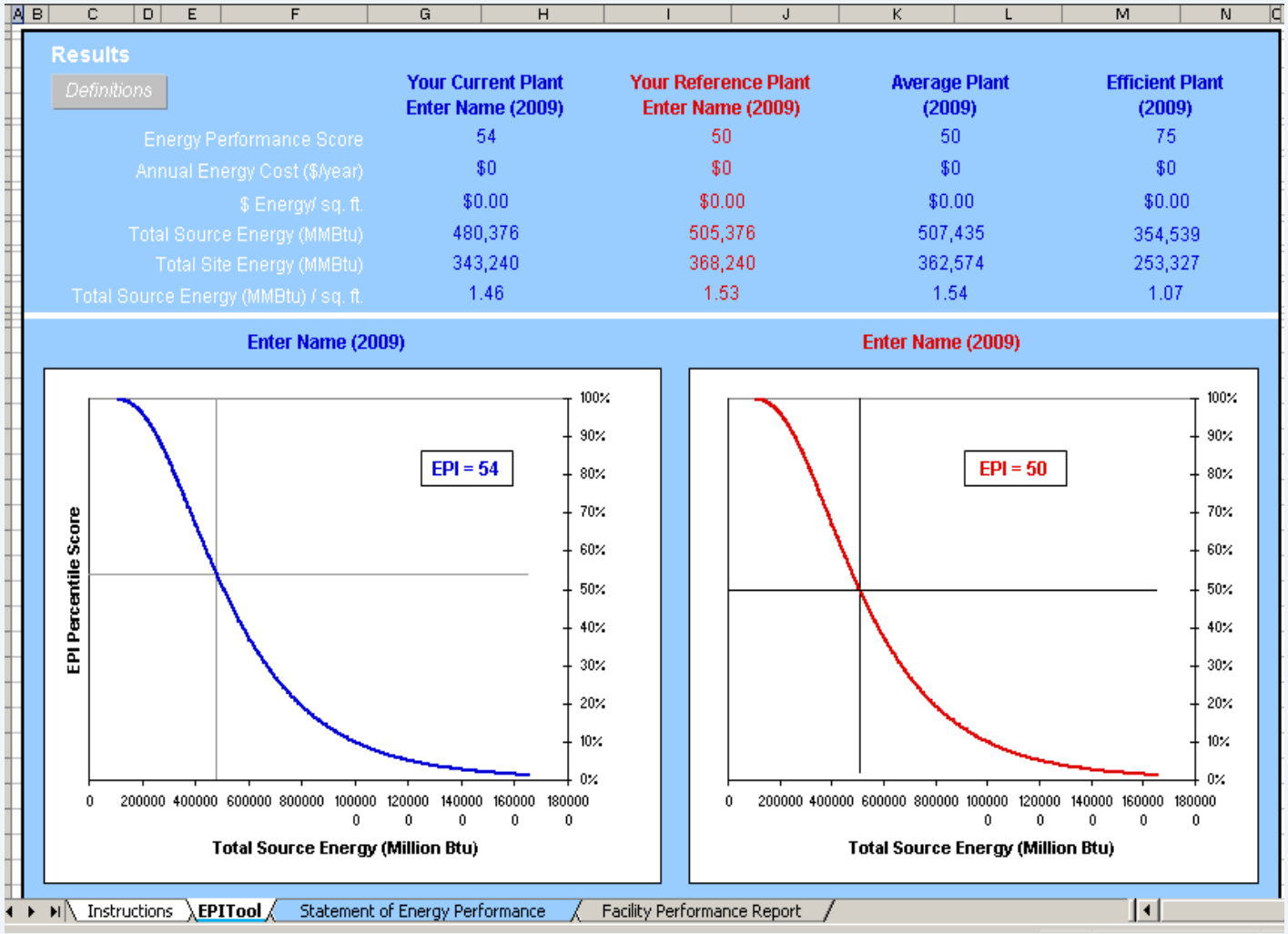
Benchmarking Tools



Set Goals

- Understand how much energy is being used, where it is being used, potential savings and put it in context
- Set a Metric
  - $500,000 per year over 3 years
  - Reduce Electricity Usage by 4,000,000 kWh per year
  - Reduce Natural Gas use by 14,000 decatherms per year
  - Reduce Water/Sewer by 11,000,000 gallons per year
  - Normalize the data

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Put it in Context

- Reduce Electric by 4,000,000 kWh per year
  - Enough electricity to power 220 houses for a year (1600-2000sq.ft)
- Reduce Natural Gas use by 14,000 decatherms per year
  - Equivalent to burning 2400 barrels of oil
- Reduce Water/Sewer by 11,000,000 gallons per year
  - Enough water to fill 18 Olympic size swimming pools

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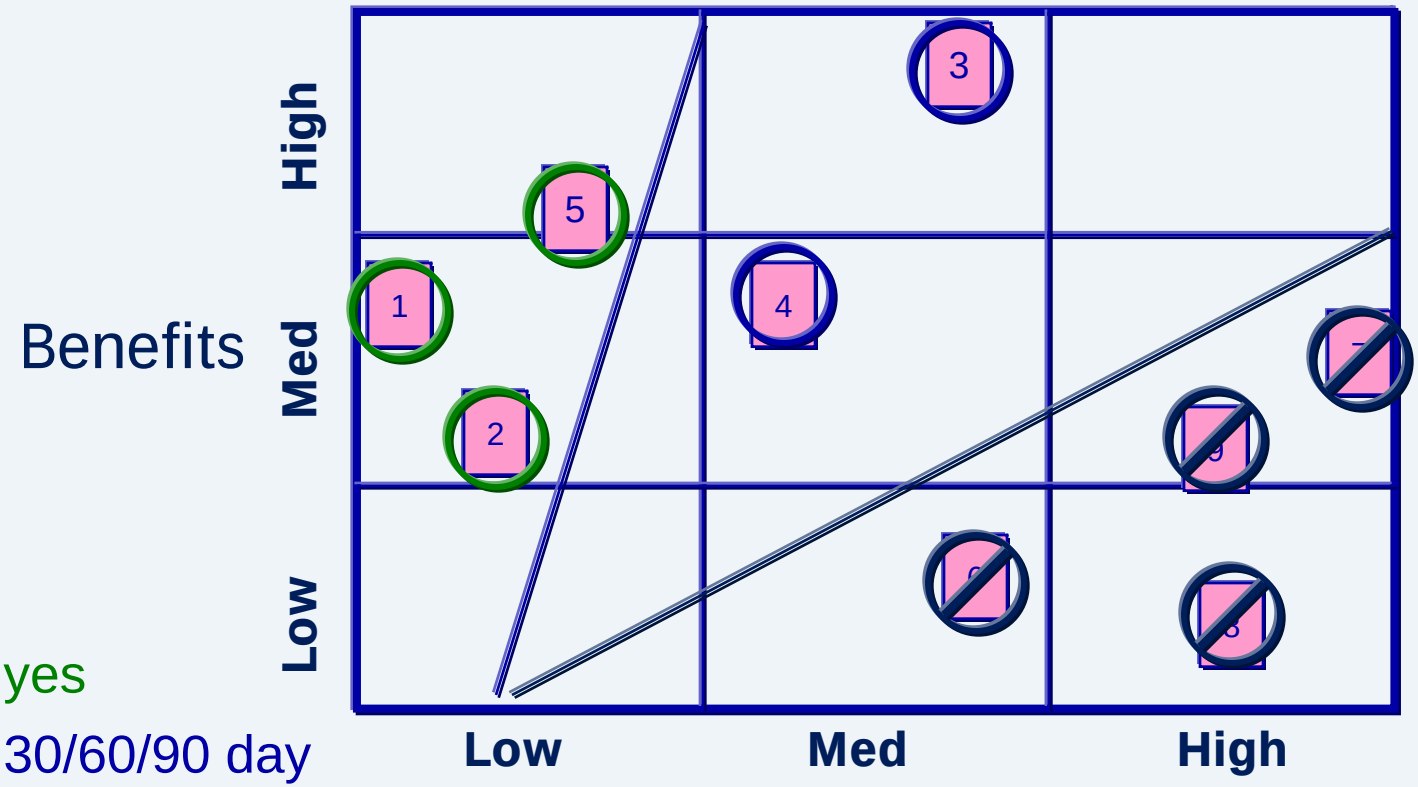
Prioritize Potential Solutions

- Place your solutions in the Effort-Benefit Grid



yes

30/60/90 day

No

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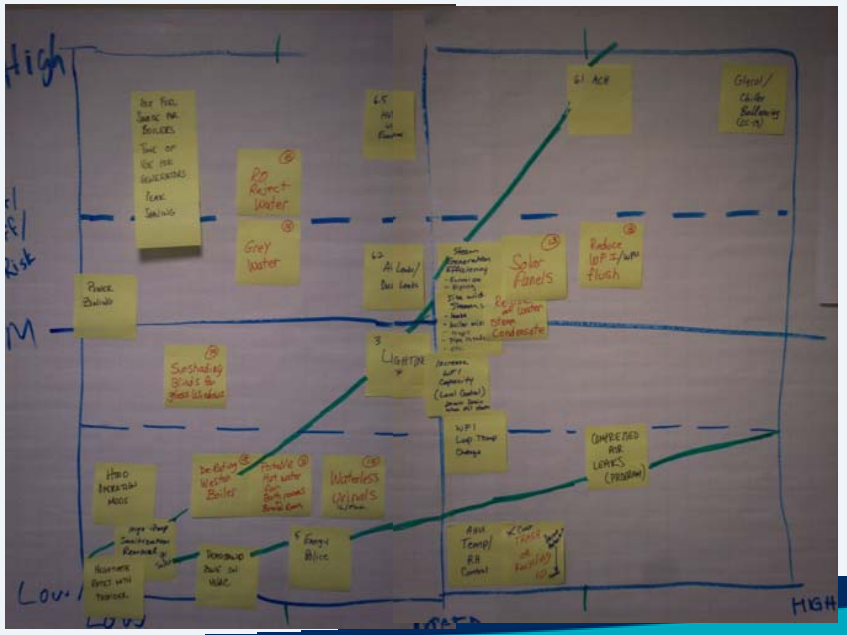
How did we do it?

- Brainstorming Sessions
- Subject Matter Experts – Voice of the Customer (VOC)
  - What does the customer need?
- Go and See
  - Walk down to see where the wastes are



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Create Action Plan

- Multigenerational Approach

Goals	Projects/ Activities	Who	2010											2011												
			Feb	Mar	April	May	June	July	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	April	May	June	July	Aug	Sept	Oct	Nov	Dec	
Generation 1 of Multigenerational Project																										
Claim the VFD Project for this project	High Level Summary of % Complete and Financial Benefit	RH																								
Steal CA project from Wilson **(Green Belt Project)**	Define																									
	Measure																									
	Analyze																									
	Improve																									
	Control																									
Quick Wins	Decon Autoclave																									
	Environmental Chambers																									
	Weston Boiler																									
Generation 1 of Multigenerational Project																										
Lighting -Energy Police	Start obtaining baseline data																									
Chiller Cooling Tower	Summarize baseline data and put together cost benefit analysis for CAPEX																									
Clean Steam System Efficiency	Start Collecting Baseline Data and Defining																									
Generation 3	Gather Baseline data for future projects																									

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Implement the Action Plan

- Setting Up the Project
  - Business Case
    - Baseline Data
  - Problem Statement
  - A3/Charter
  - Lean Six Sigma
  - DMAIC (Define, Measure, Analyze, Improve, Control)
  - Kaizen
  - Just Do It – Low hanging fruit

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SIPOC

S	I	P	O	C
•Electric Company •Air Equipment •Water Company	•Electricity •Water for Cooling •Air Demand	1. Electricity 2. Compressors 3. Driers 4. Distribution 5. Use	•Clean Air •Instrument Air •Plant Air	•User •Equip/ Process •Budget holder

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Compressed Air Example

- Define the System
  - Compressed Air Audit
  - Compressor Information
    - Full Load HP
    - Partial Load HP
  - Type of Compressor
    - Centrifugal, Rotary, Reciprocating
  - Type of Dryer
    - Refrigerator, desiccant, heat of compression
  - Compressor Control
  - Current Supply Pressure
  - Minimum Acceptable Pressure

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Inventory Equipment

Equipment Number	KM-8501			Year Installed	6/1/2002	
Manufacturer	Kobelco	SN	06J0419	Model	KNW 0-D/L	
Rated Capacity	332	CFM at	110	Psig	3550	RPM
Motor Rating	75	Hp	460	Voltage	104	Amps
Brake horse Power	83	BHP at	110	psig		
Condition:	Motor Efficiency 94.5%...Need performance curve.					

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Evaluate Progress

- Measurement System Analysis
  - Our ability to assess the performance of a process is only as good as our ability to measure it
  - The measurement system is the ‘eye” of the process
  - Identify and filter your X’s (outputs)
  - Which Y’s (inputs) impact your X’s

X’s and Y’s

- Outputs
  - Dew point
  - PRV Set Point
  - PSV Set Point
  - CA Required Set Point
  - Alarms
  - Compressor Temperature
  - Temperature
  - Pressure
  - Leaks
  - Cost
  - Run time
  - Full/Half/No Load Time
  - Control Strategy
  - Compressor Capacity
  - Air inlet temp
  - Air inlet pressure
  - Air outlet pressure
  - Cooling water temp
  - Air dew point temp
  - Evaporator press
- Inputs
  - Cooling Water Temp
  - Intake Air Temperature
  - Electricity

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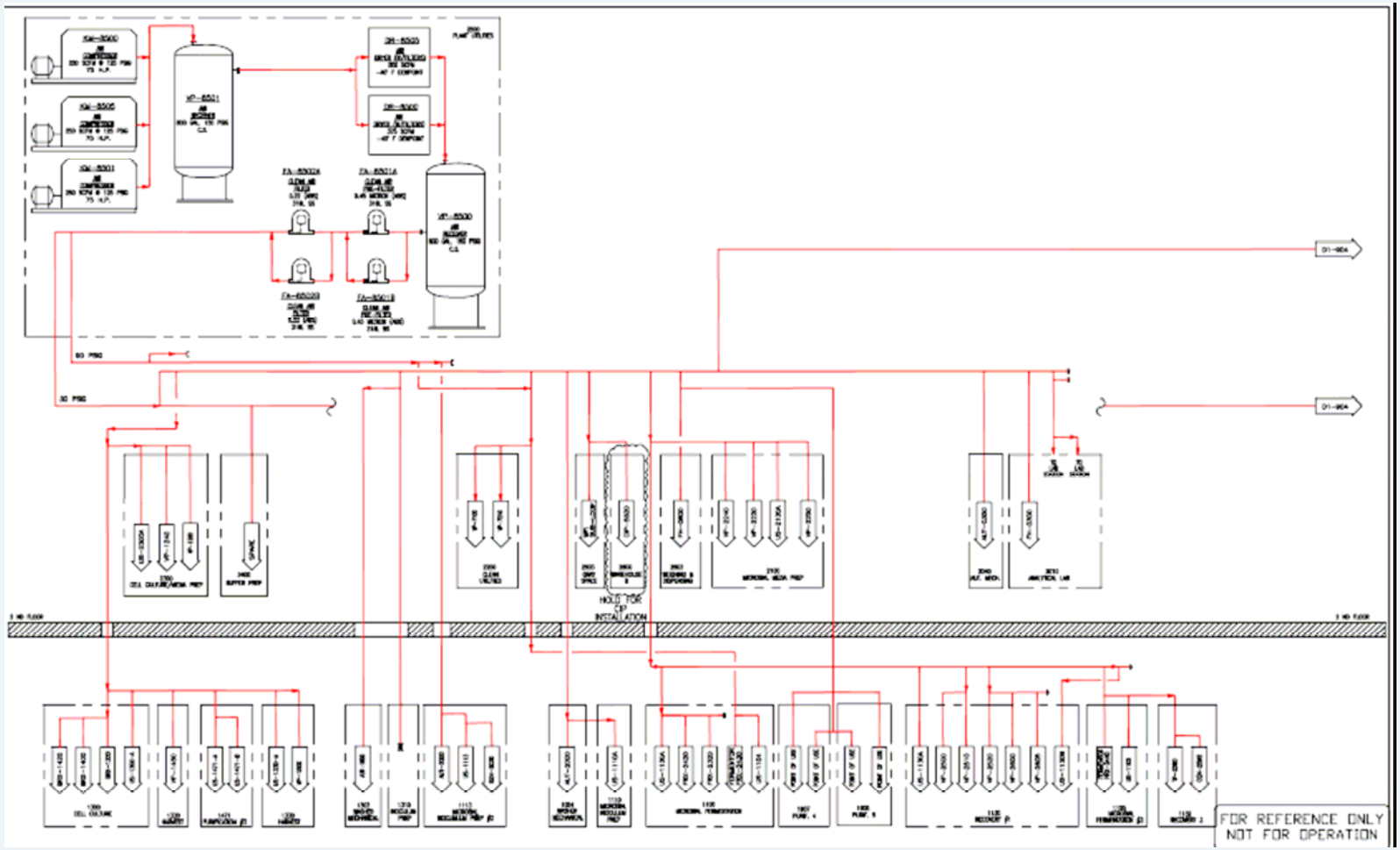
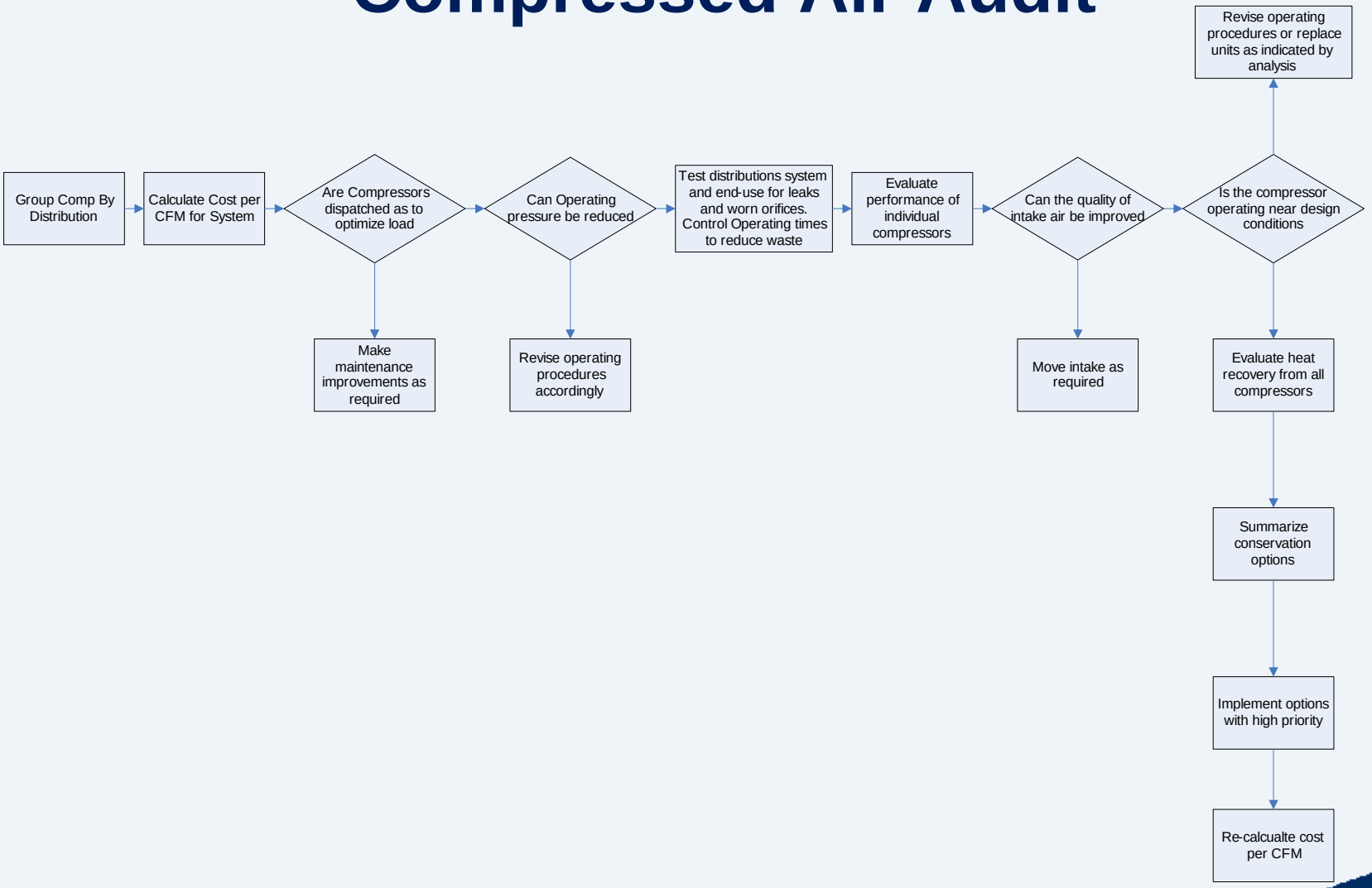
Detailed Process Map



Compressed Air Audit



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Data Collection Plan

- 3 Compressors
- Loaded Hours
- Unloaded Hours
- Loaded Amps
- Unloaded Amps
- Loaded KwH
- Unloaded kWH
- Calculate $/CF

FOR MONTH/YEAR OF _____ AIR COMPRESSOR # _____

Date	Inter Cooler Drain	After Cooler Drain	Air Filter Cond.	Oil Filter Cond.	Oil Level	1st Stage Discharge Air Pressure Load	1st Stage Discharge Air Pressure Unload	2nd Stage Discharge Air Press.	Lube Oil Press	1st Stage Disch Temp	2nd Stage Disch Temp	2nd Stage Suction Temp	Disch Temp	Lube Oil Temp	Run Hour	Loaded Hours	Initials
1																	
2																	
3																	

Summary of Data Collection

8500	Loaded Amps	Unloaded Amps	Loaded KW	Unloaded KW	Loaded Hours	Unloaded Hours	KWH/ Month	Cost/ Month
May	81	17	60.61	12.72	215	87	15765.08	1075.34
June	81	17	60.61	12.72	308	104	22584.39	1540.48
July	81	17	60.61	12.72	178	112	13052.02	890.28
August	81	17	60.61	12.72	329	104.5	24124.24	1645.51
8501	Loaded Amps	Unloaded Amps	Loaded KW	Unloaded KW	Loaded Hours	Unloaded Hours	KWH/ Month	Cost/ Month
May	89	18	66.59	13.47	169	78	13530.13	922.89
June	89	18	66.59	13.47	101	123	8086.06	552.36
July	89	18	66.59	13.47	277.4	87.6	22208.64	1517.07
8505	Loaded Amps	Unloaded Amps	Loaded KW	Unloaded KW	Loaded Hours	Unloaded Hours	KWH/ Month	Cost/ Month
May	81	17	60.61	12.72	240	121	17598.23	1200.38
June	81	17	60.61	12.72	285	58	20897.90	1425.45
July	81	17	60.61	12.72	272	109	19944.66	1360.43
August	81	17	60.61	12.72	379.2	148	27805.20	1896.59

May-Aug	48,956,544 CF	$14,027
Average	12,239,136 CF	$3,507
Annual Cost based on Average	146,869,632 CF Annual	$42,080
Cost per 1000 CF		$0.29

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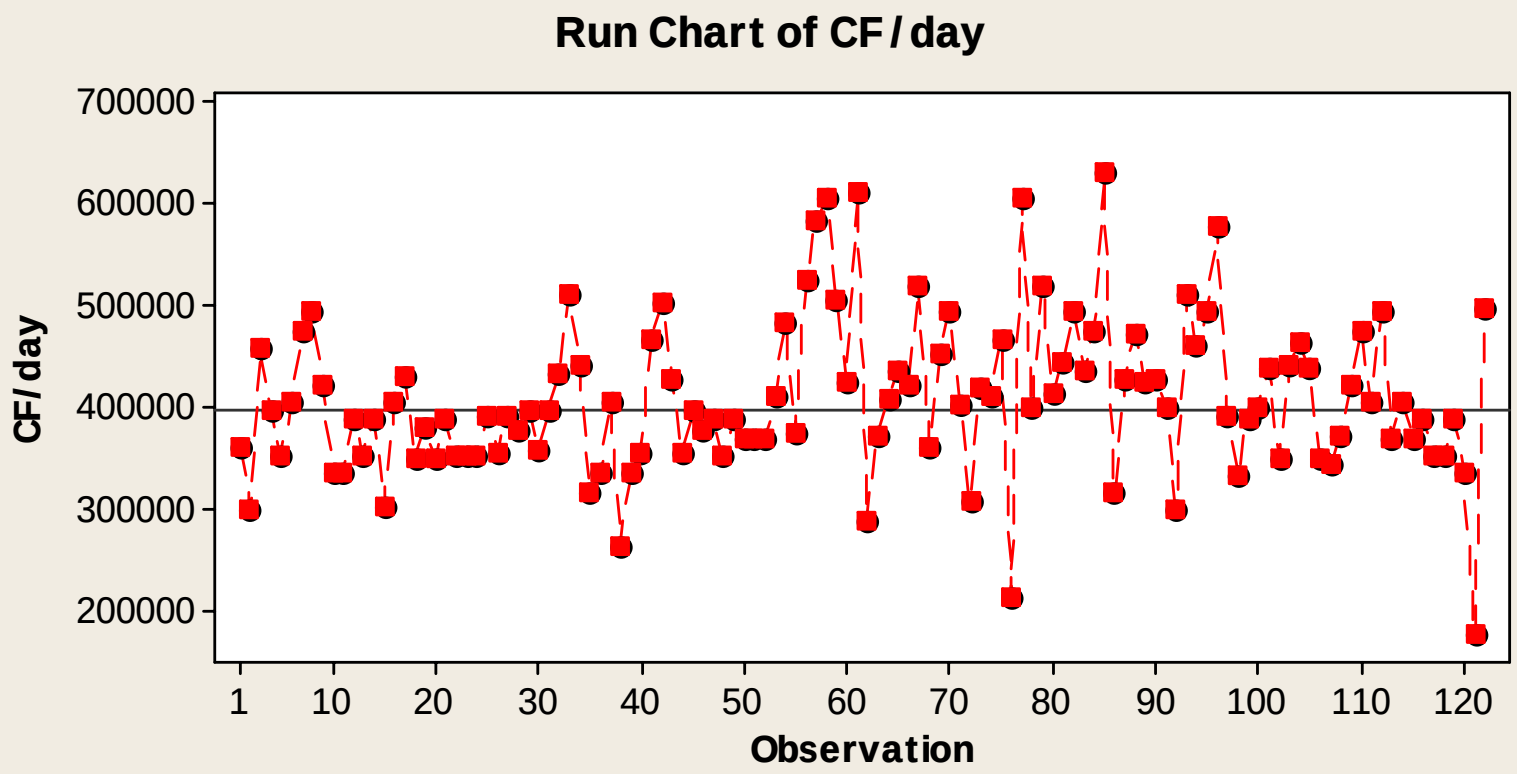
Run Chart of CF/Day



Number of runs about median:	38
Expected number of runs:	62.0
Longest run about median:	14
Approx P-Value for Clustering:	0.000
Approx P-Value for Mixtures:	1.000

Number of runs up or down:	80
Expected number of runs:	81.0
Longest run up or down:	4
Approx P-Value for Trends:	0.414
Approx P-Value for Oscillation:	0.586

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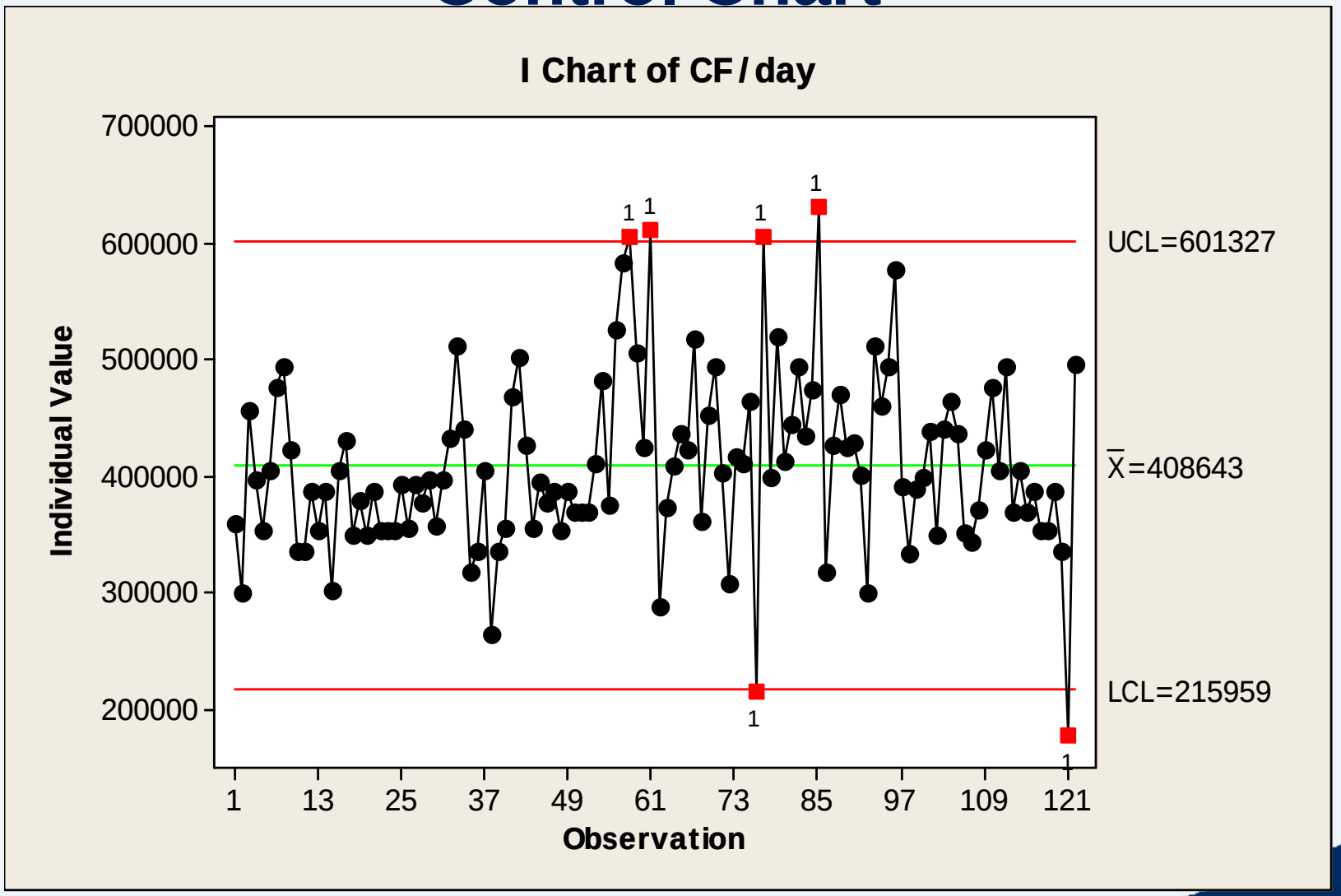
Control Chart



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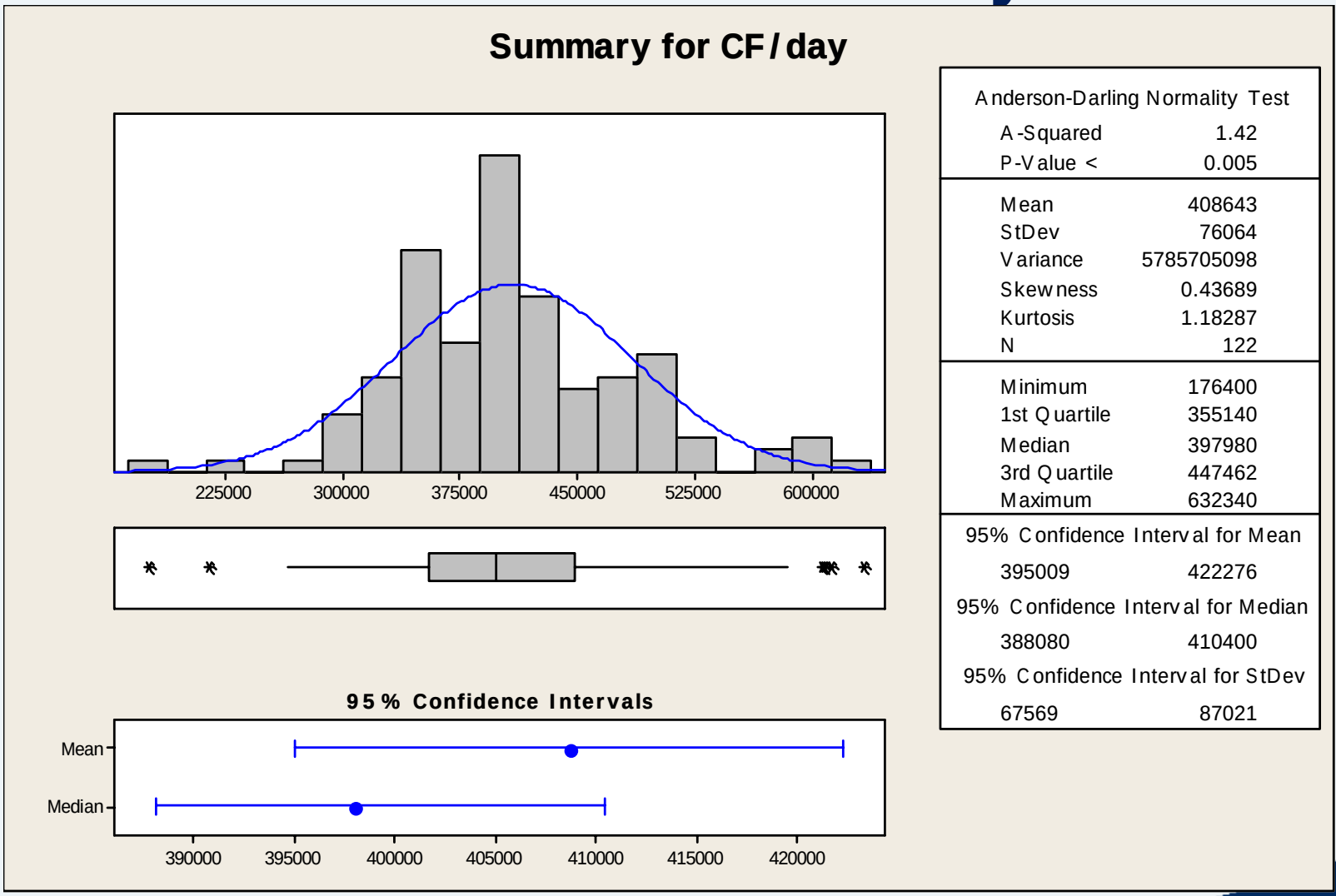
Statistical Summary



Anderson-Darling Normality Test	
A-Squared	1.42
P-Value <	0.005
Mean	408643
StDev	76064
Variance	5785705098
Skewness	0.43689
Kurtosis	1.18287
N	122
Minimum	176400
1st Quartile	355140
Median	397980
3rd Quartile	447462
Maximum	632340
95% Confidence Interval for Mean	
395009	422276
95% Confidence Interval for Median	
388080	410400
95% Confidence Interval for StDev	
67569	87021

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Compressed Air Audits

Based on a review of widely available industry literature below are the most common, highest-payback problems typically found during a professional audit of CA systems:

- ***(1) Leaks***
- ***(2) Overpressurization***
- ***(3) Double-Check Air Requirements***
- ***(4) Angle Connections***
- ***(5) Bad Piping***
- ***(6) Obsolete Restrictions***
- ***(7) Insufficient Storage***
- ***(8) Inappropriate Use***
- ***(9) Pumps***
- ***(10) Maintain the System***

Leak Survey

Date Leak Discovered	Location Description	Approximate Pipe/Tubing Size	Nuisance or Significant (If Significant submit SRF)	Leak Discovered by Initials

Was the leak repaired?	Yes / No (Circle one)	SRF # if Applicable	

Comments:

Administration

Leak #		Date Leak Fixed		Approximate Leak Size	

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Analyze

- Total # of Leaks Found
  - Estimated/Measure Loss in system
- Overpressurization
  - Can you reduce pressure based on actual requirements?
- Air Requirements
  - Dew points, Control strategy, etc.
- Inappropriate Use
  - Address the inappropriate uses in SOPs
- Maintain the System
  - PMs, etc.

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Improve

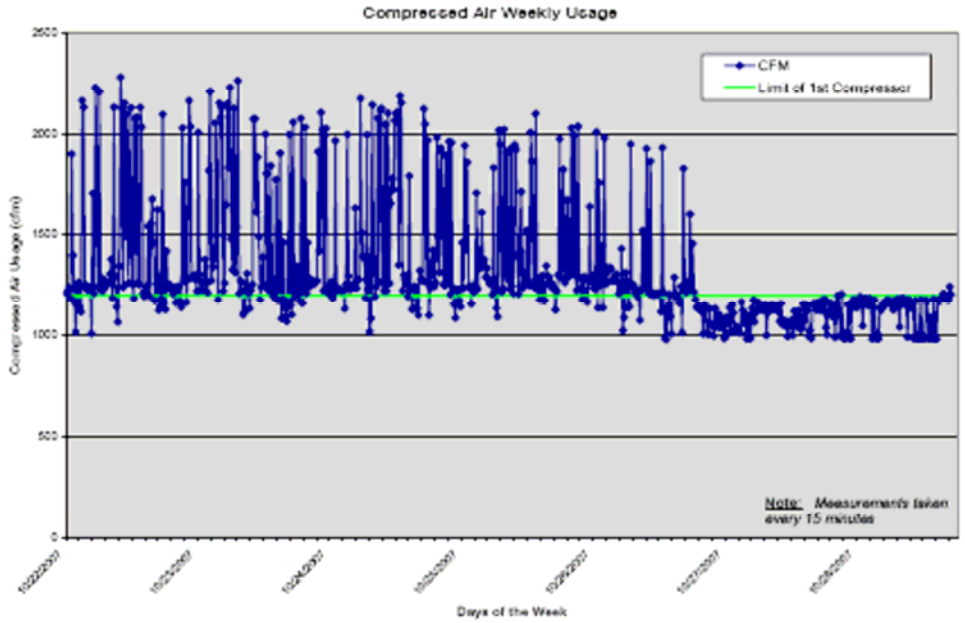
- On-going
- Comprehensive leak detection program
- Compressed air requirements, both pressure (psi) and demand
- Cfm supply vs. demand
- Fix leaks
- Adjust others

Control

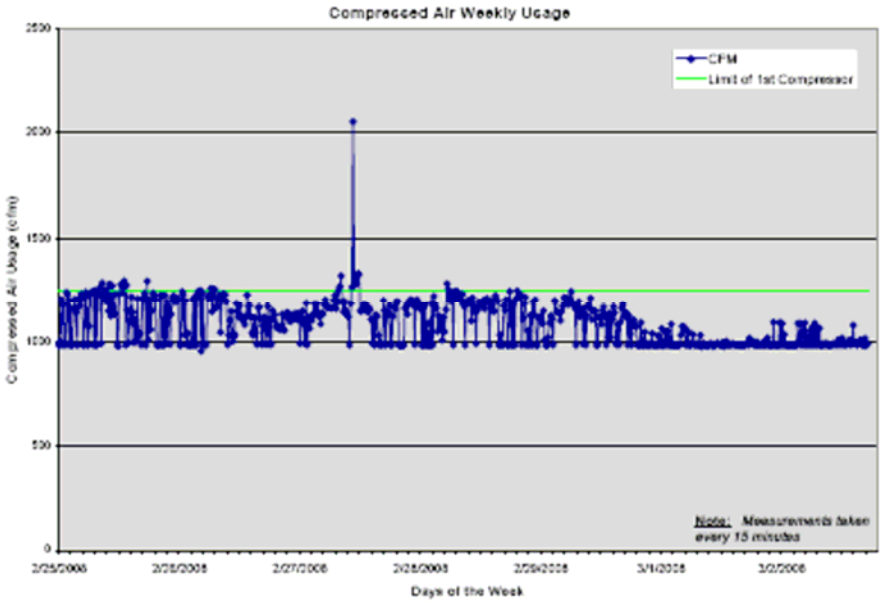
- Re-measure
- Mistake Proof – Standardize the work
- Leak Detector Equipment
- PMs
- Education
- Update SOPs
- Install Meters

Merck Wilson (Before & After)

Before



After



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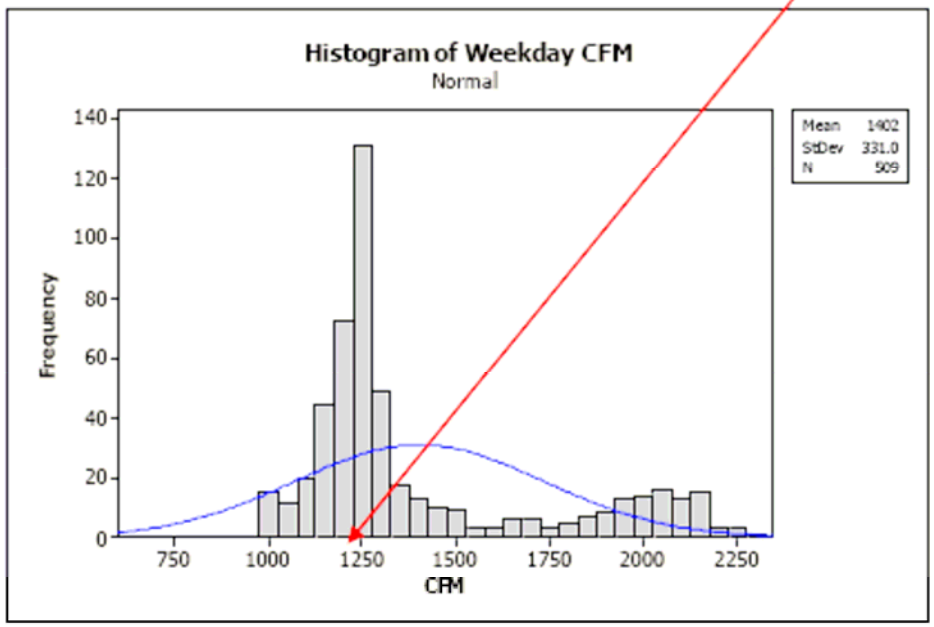
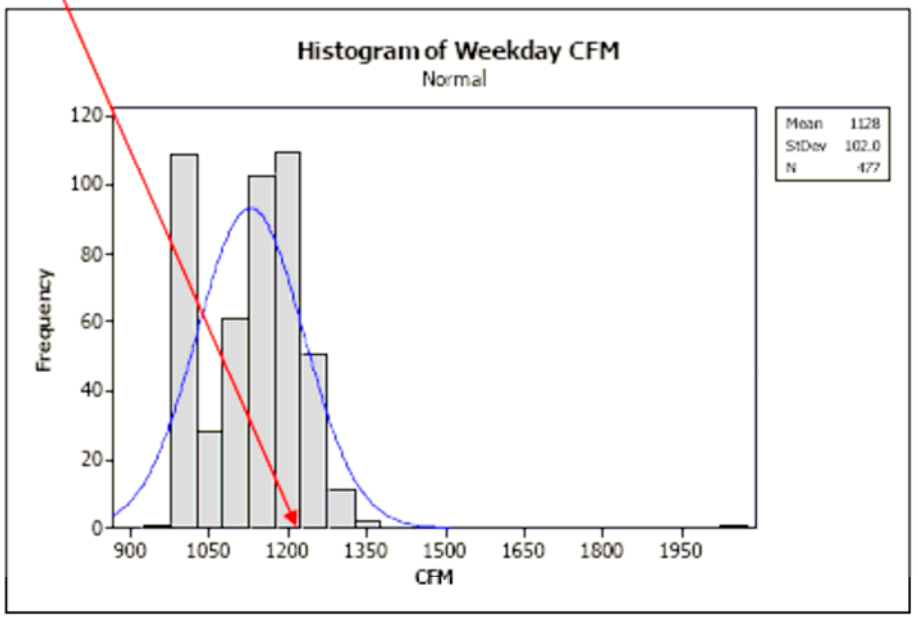
Merck Wilson (Before & After)

Limit of 1st Compressor

Before



After



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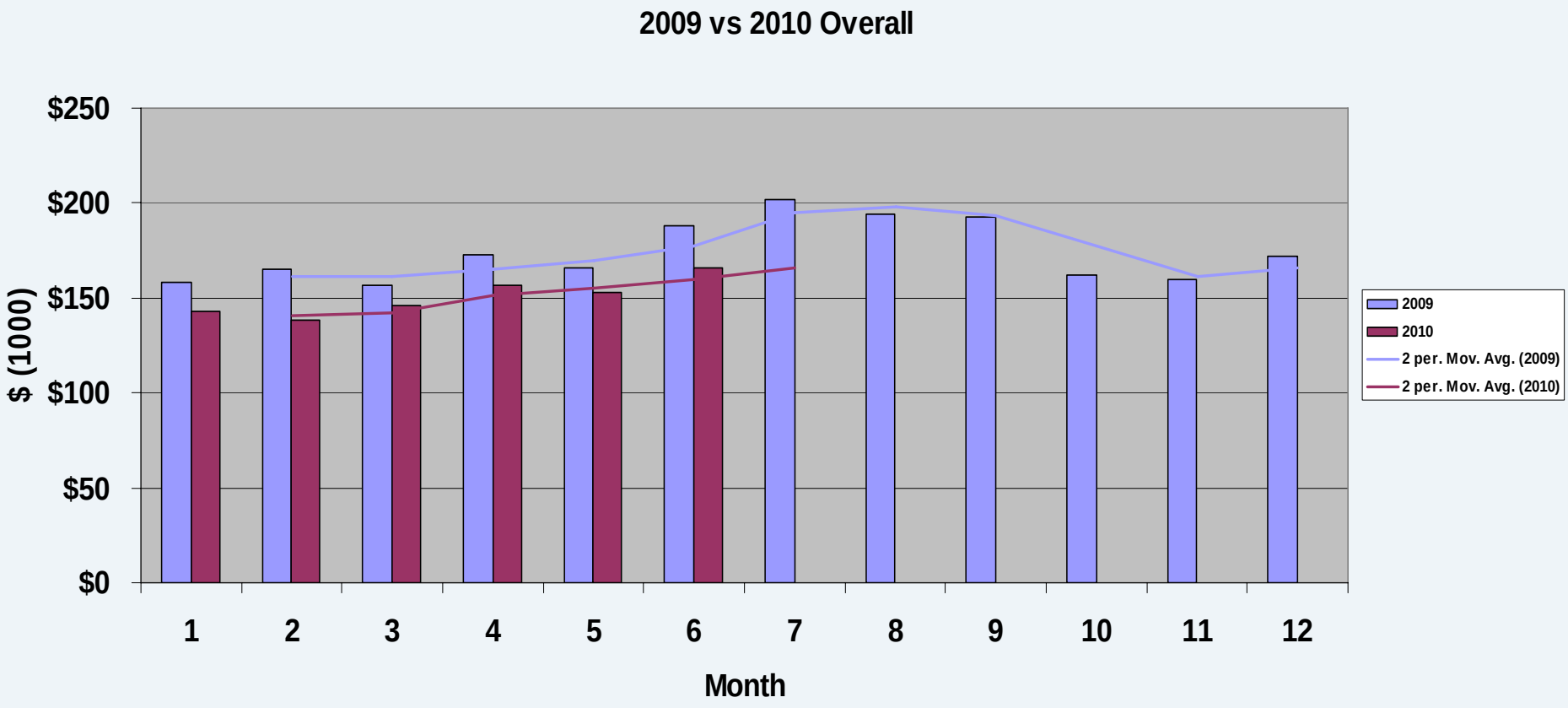
Evaluation – 2009 vs 2010



Recognize Achievements

- VFD Project
  - $100,000 savings/yr
- Weston Boiler
  - ~$9,000/yr and 9 metric tons of CO2
- Compressed Air
  - DMAIC project, currently in Analyze Phase
- Lighting
  - Proposed $50K savings per year, ~ 500 metric tons of CO2
- Energy Awareness – Think Energy!

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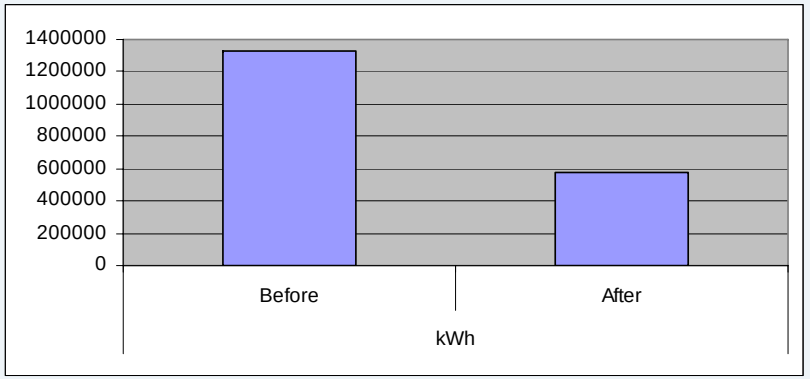
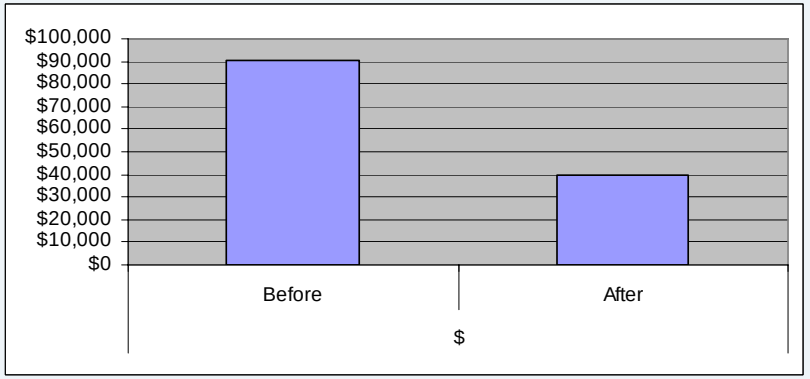
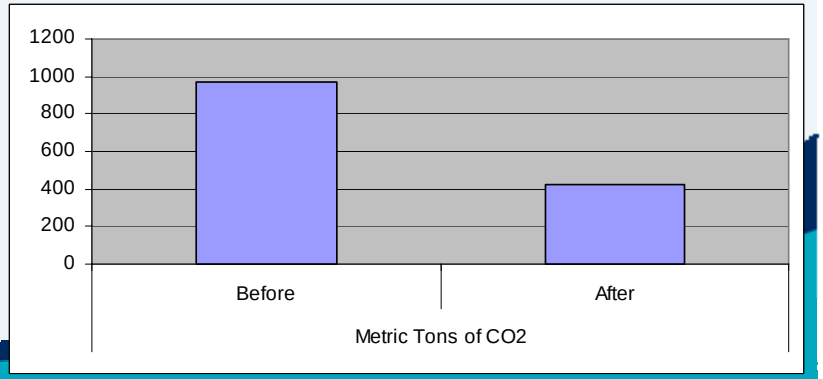
Reducing CO2 Emissions Example

- 10% of the electricity used in our Man. Facility is from the lighting
- Program to retrofit fixtures throughout facility to more efficient lamps and ballasts
- Reduce electricity used by 749,000 kWh
- Reduce cost by >$50,000
- Reduce CO2 emissions by > 500 Metric Tons







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Sustaining the Gains

- **Education/Awareness**
  - **Business**
    - **Make Energy Awareness part of the business plan**
  - **People**
    - **Think Energy!**
  - **Process**
    - **Incorporate Energy Awareness into planning and operating procedures**
  - **Capital**
    - **Address Energy Awareness as part of Capital Investment Plan**

www.energystar.gov/ia/business/guidelines/assessment_matrix.xls

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Establish Best Practices

- Administration
- Lighting
- Utilities
- Process Applications
- Misc Mechanical
- HVAC
- Electric
- Architectural

Challenges and Lessons Learned

- Be prepared
- Sponsorship is key
- Don’t count on the money
- Change is hard
- QA and Compliance implications
- Time

Conclusion

- Change the Culture
  - Commit to Continuous Improvement
- Assess Performance
- Identify Savings Potential by Benchmarking
- Set Goals
- Create Action Plan
  - Brainstorming, VOC, Best Practices, Prioritize

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Conclusion (Cont.)

- Implement the Action Plan
- Tackle the Project
  - Define, Measure, Analyze, Improve, Sustain
- Evaluate Progress
  - Monitor/Re-Assess
- Recognize Achievements
- Sustaining the Gains

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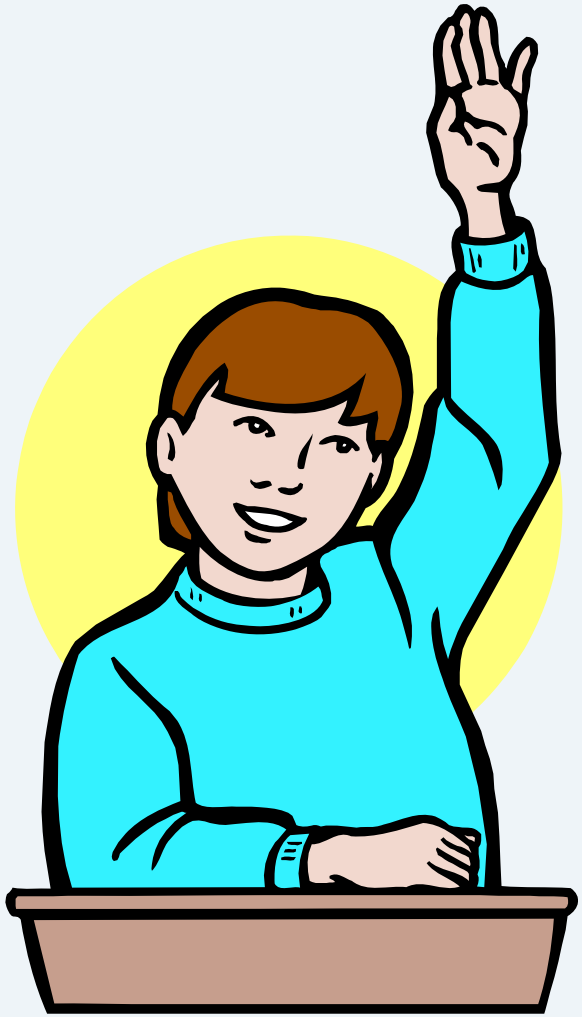
Questions?



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