Chemometrics in Process Analytical Technology (PAT)- A Six Sigma Perspective

Charles E. (Chuck) Miller, Ph.D.

Eigenvector Research, Inc.

EIGENVECTOR RESEARCH INCORPORATED

DUPONT

The miracles of science™

SIX SIGMA CERTIFICATE

Charles E. Miller

OF GLOBAL SERVICES

is hereby certified as a Global Services Six Sigma Green Belt after having completed training and Project Requirements.

Master Black Belt

James B. Porter, Jr. – Vice President-Engineering and Operations

Certification Date
December 17, 2003

EIGENVECTOR RESEARCH INCORPORATED

2

Why this talk?

- I like to talk about process analytical chemistry (PAT) and chemometrics a lot
- Concepts from Six Sigma training often "creep" into the discussion
- Explore the relationship between Six Sigma (6σ), PAT, and chemometrics

3

Outline

- Introduction to Six-Sigma (6σ)
- Relationships: 6σ, PAT, Chemometrics
- What can Six-Sigma bring to PAT, Chemometrics?
- Summary

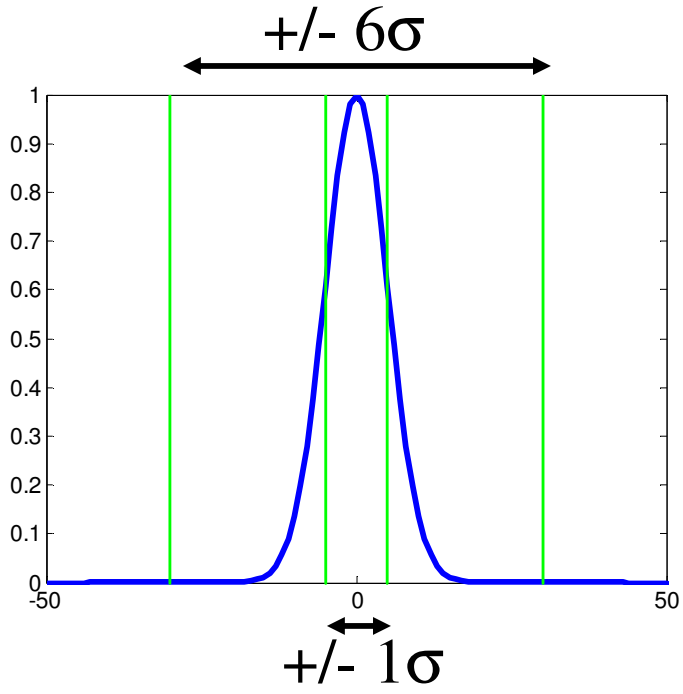
(to be continued…)

EIGENVECTOR RESEARCH INCORPORATED

4

Six Sigma (6σ)

- A process improvement program
- Formulated in 1986, for Motorola
  - Heavily influenced by teachings of Shewhart, Deming, Taguchi, Ishikawa, Juran, and others
- By 2000: ~2/3 of Fortune 500
  - DuPont – since 1998
- Summarize into four components:
  - A PROCESS,
  - A TOOLKIT,
  - AN INFRASTRUCTURE, and…
  - A PHILOSOPHY!



Technical definition:
3.4 defects per million opportunities

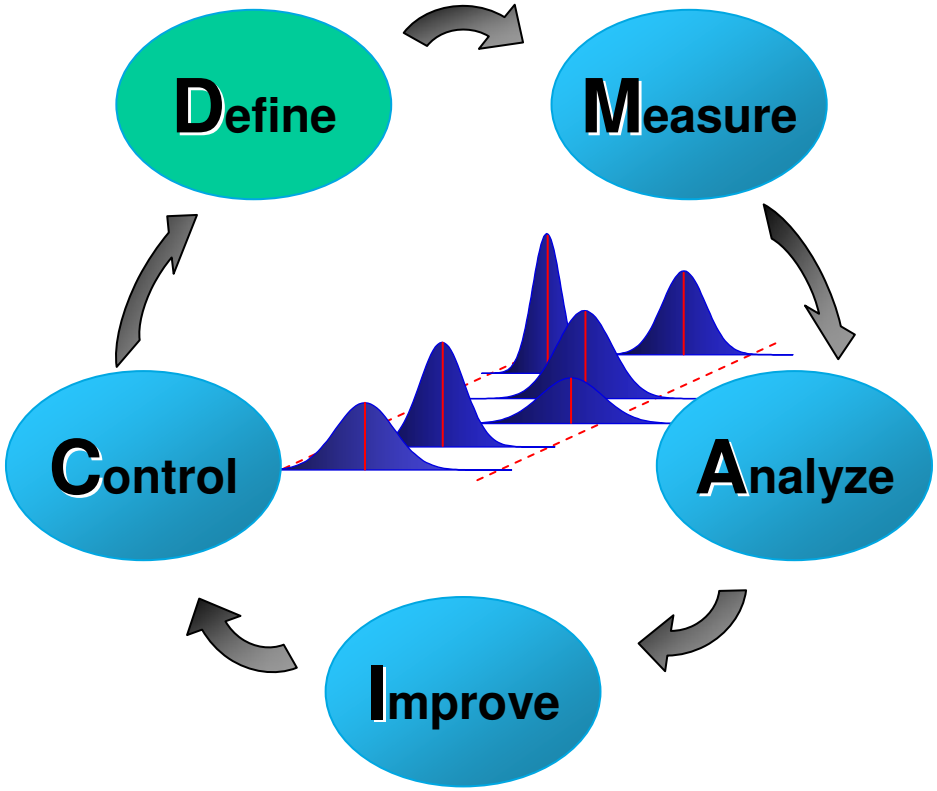
Ref: http://www.sixsigmacompanies.com

EIGENVECTOR RESEARCH INCORPORATED

5

The Six-Sigma Process: *"DMAIC"*

- NOT LINEAR!
  - Often backtrack
- Similar process ("DMADV"), for R&D projects



EIGENVECTOR RESEARCH INCORPORATED

6

The Six Sigma Toolkit

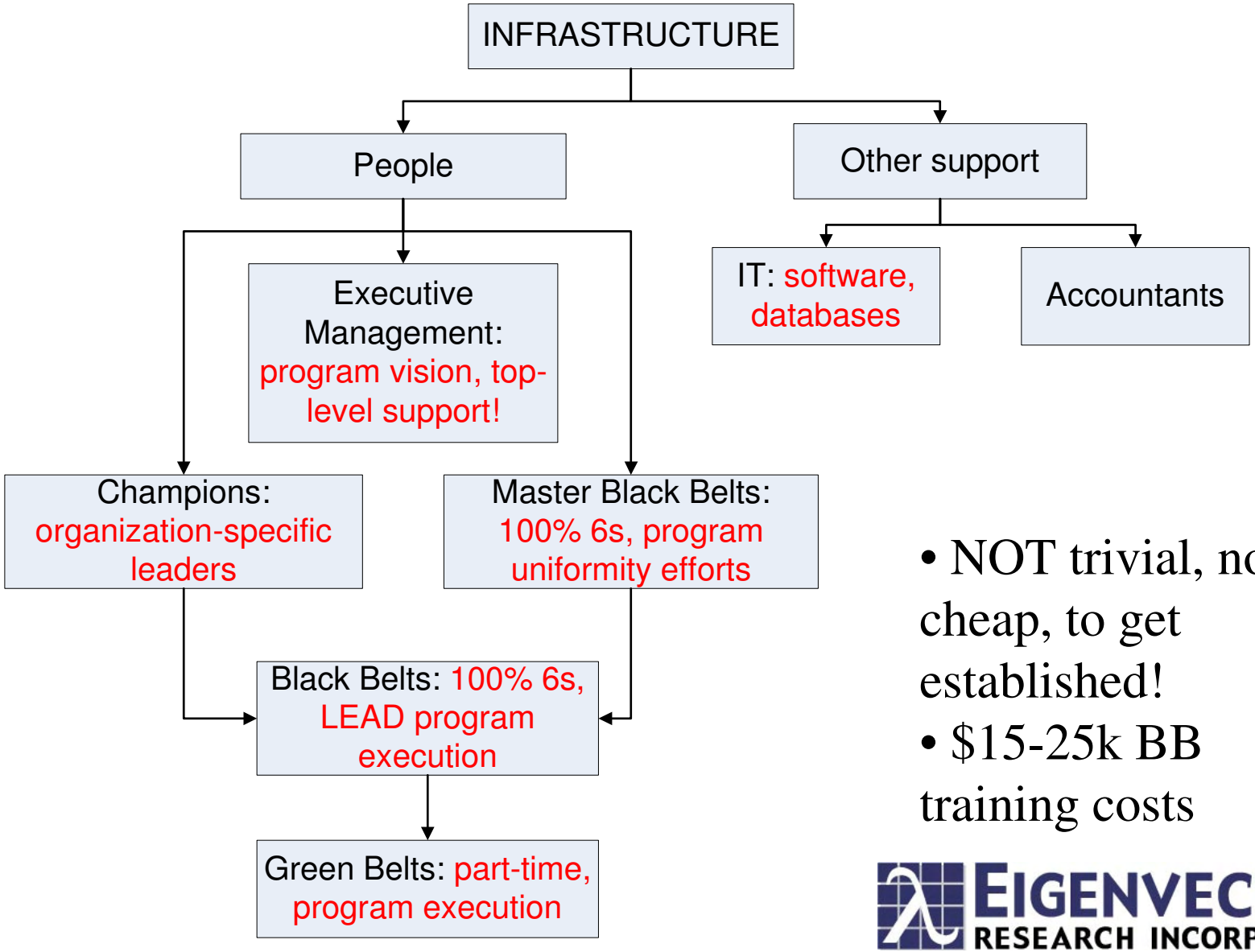
- Statistical tools
  - Design of Experiments
  - "Classical" Data analysis (i.e., ANOVA, linear regression)
- Organizational Tools
  - Process mapping, brainstorming
  - Templates/guides
  - Risk Management

(punch line forthcoming…)

EIGENVECTOR RESEARCH INCORPORATED

7

The Six Sigma Infrastructure



- NOT trivial, nor cheap, to get established!
- $15-25k BB training costs

EIGENVECTOR RESEARCH INCORPORATED

8

The Six Sigma Philosophy

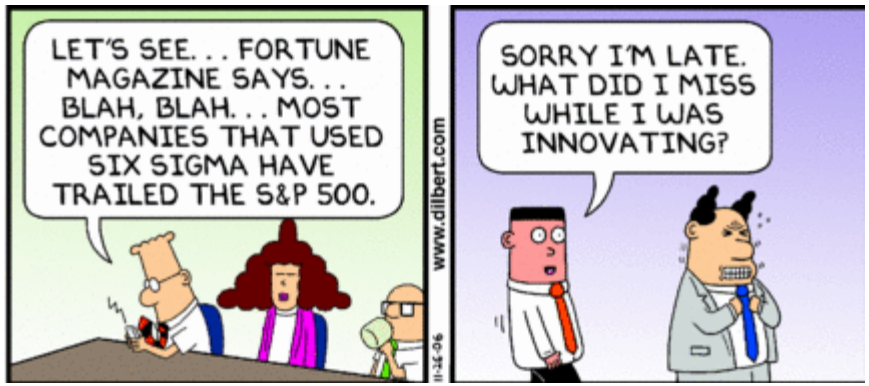
- **Data**-driven decision making
  - vs. Folklore-driven
- ***Real* financial verification** of a project's impact
  - Validated by accountants (vs. "handwaving")
  - Comparable between functions, departments
- **Strong, Top-down** management support

EIGENVECTOR RESEARCH INCORPORATED

9

Six-Sigma Detractors

- Another one of those "bogus" programs?
- Charles Holland (Qualpro)
  - 54 of 58 "large companies" implementing it are "lagging behind" in S&P 500
- Other criticisms
  - Stifles creativity, innovation
  - Offers nothing new
  - Too "inward looking"



http://money.cnn.com/2006/07/10/magazines/fortune/rule4.fortune/index.htm

EIGENVECTOR RESEARCH INCORPORATED

10

But, it's NOT going away!

- Now, 100s of companies utilizing it
  - At least 100 in current Fortune 500
  - US Military
  - Wide diversity of business segments
- WHY the traction?
  - Toolkit rather similar to TQM, other previous efforts, BUT…

    - Better use of resources
    - Different corporate attitude
    - Easier project vs. project comparison

Ref: http://www.sixsigmacompanies.com, *and* http://www.isixsigma.com/library/content/c010723a.asp

EIGENVECTOR RESEARCH INCORPORATED

11

Relationship: PAT and Chemometrics

Enabling technology for **multivariate** PAT (NIR, Raman, FTIR..)

Exploratory tools (MCR) support PAT scouting!

Supports process modeling/simulation- to show PAT value!

Chemometrics

PAT

High-value chemometrics deployment opportunities!

EIGENVECTOR RESEARCH INCORPORATED

12

Relationships: PAT, Chemometrics, 6σ

Multivariate data analysis toolset (cluster analysis, variable selection, cross-validation)

Chemometrics

Empirical modeling philosophy

6σ

PAT

High-frequency, high-relevance DATA!

EIGENVECTOR RESEARCH INCORPORATED

13

Relationships: PAT, Chemometrics, 6σ

Chemometrics

6σ

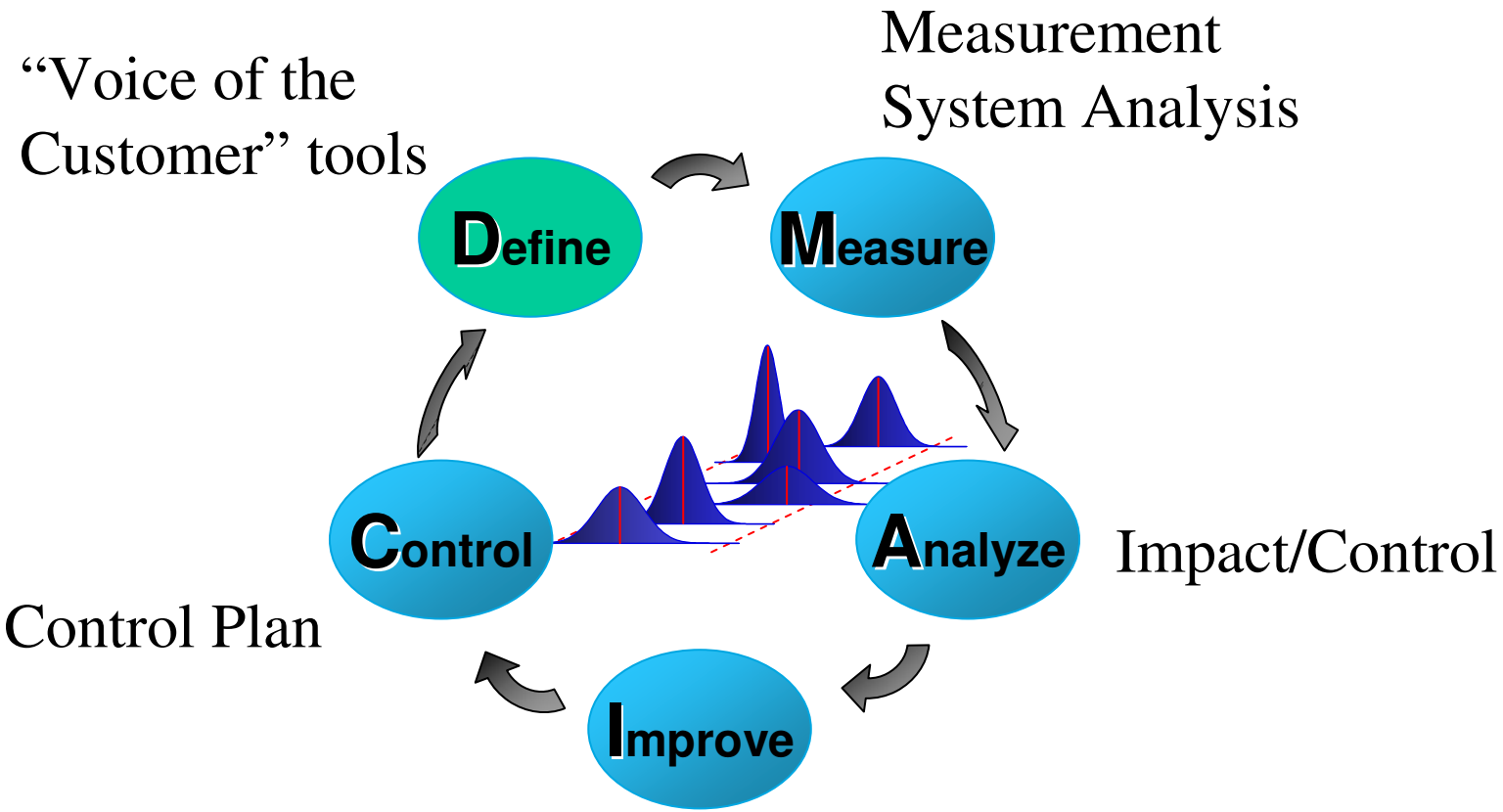
BUT…
What does Six-Sigma bring to Chemometrics/PAT???...

PAT

EIGENVECTOR RESEARCH INCORPORATED

14

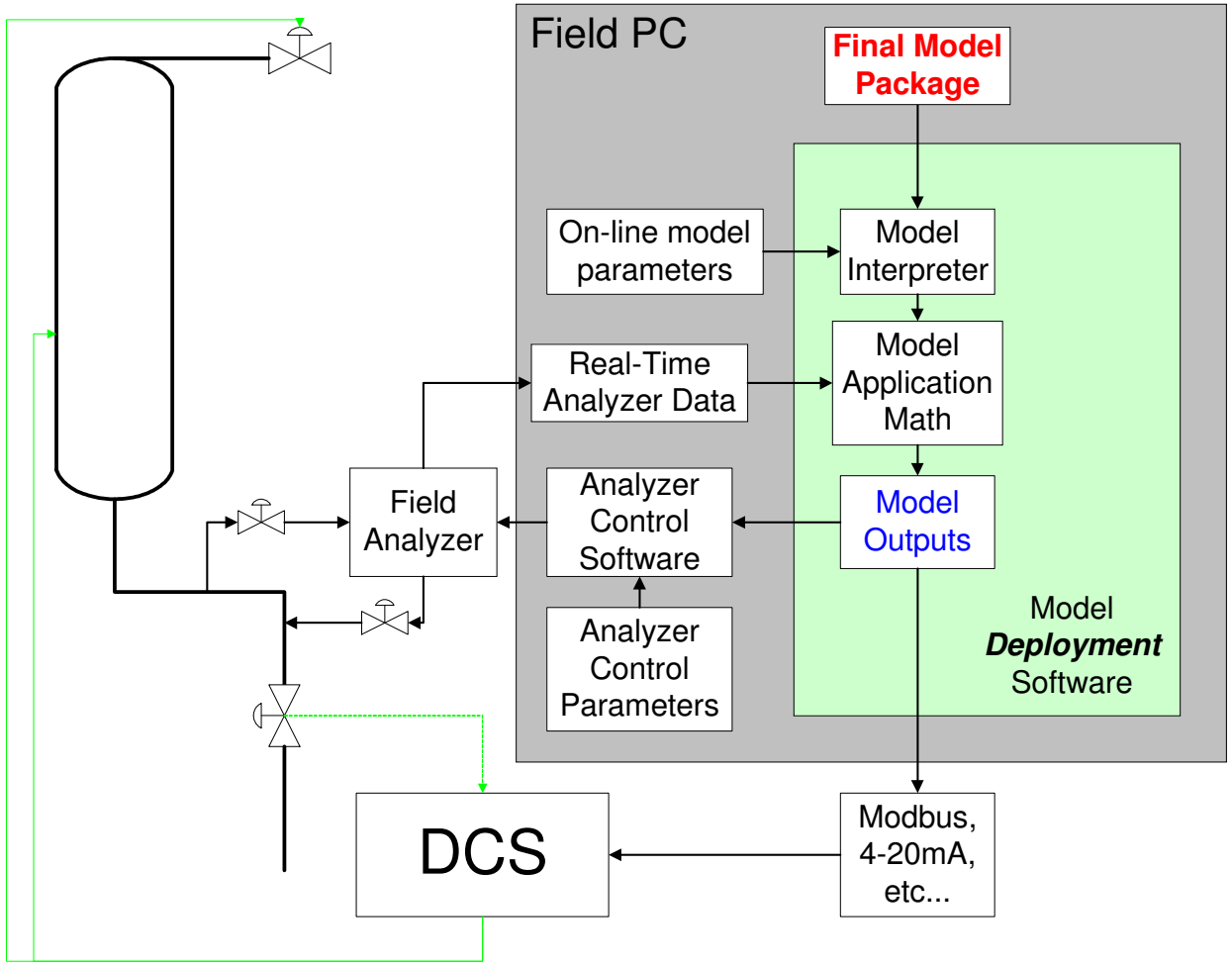
How Six Sigma can help Chemometrics/PAT



EIGENVECTOR RESEARCH INCORPORATED

15

PAT/Chemometrics Scenario



Existing PAT/Chemometrics application

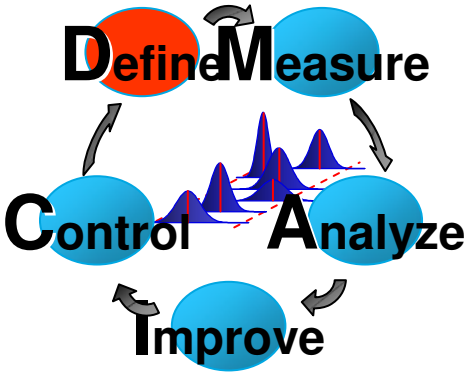
"Not performing well-enough" to be useful

The plant might "scrap it"

EIGENVECTOR RESEARCH INCORPORATED

16

Define: Voice of the Customer



- **Define Phase:**
  - **Time-saving** project phase
  - Problem definition/information-gathering
  - Get the "Voice of the Customer"
- Seems trivial, but
  - **WHO** are the customers?
  - **HOW** do you get their "voice"?
  - **WHAT** questions do you ask them?
  - **HOW** do you "process" their responses?
- Interpersonal skills
  - BE ANNOYING, PERSISTANT!

EIGENVECTOR RESEARCH INCORPORATED

17

WHO are the customers?

Process engineers

Chemometrics Software Users?

Process operators

Operations Management

Maintenance Technicians

Project Engineers

WHAT do I ask them?:

- what precision is required of the analyzer?
- can calibration samples be extracted from the process?
- how often does the sampling system “foul”?
- are analyzer outputs useful during product transitions?

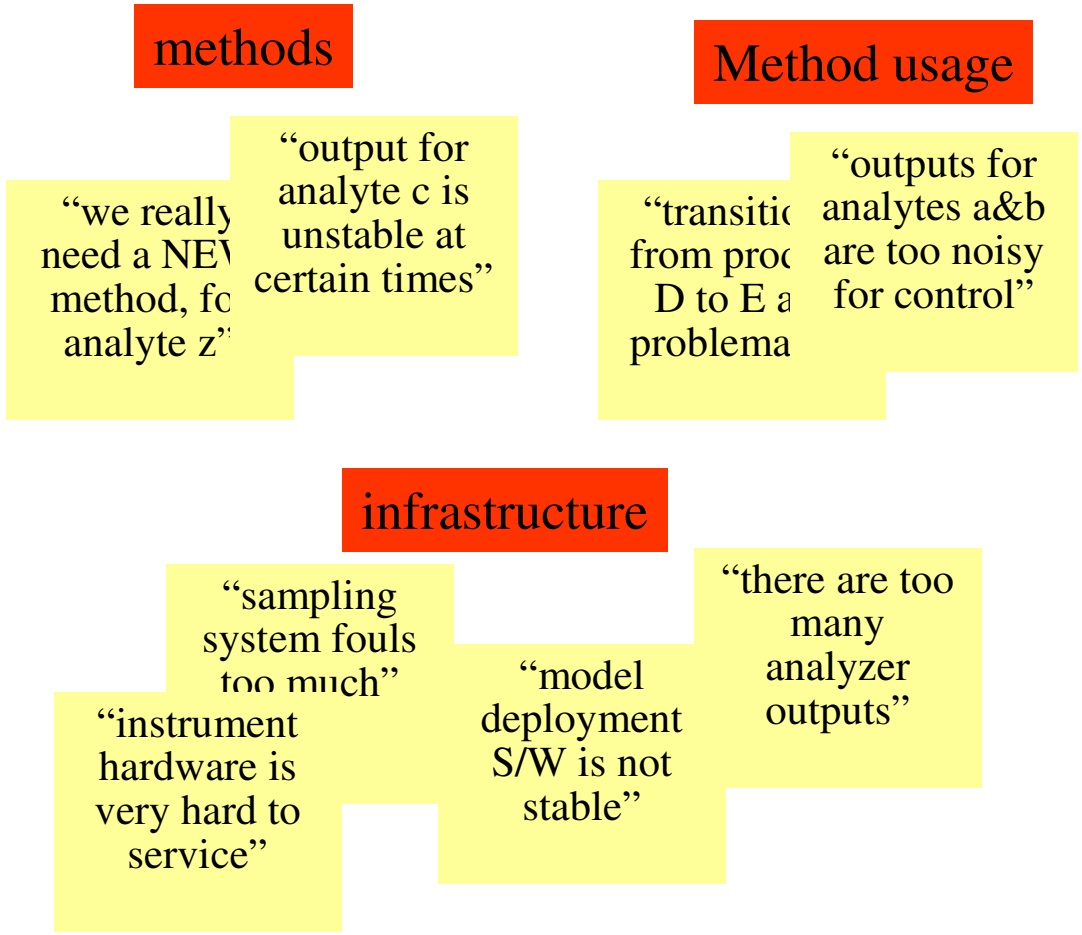
EIGENVECTOR RESEARCH INCORPORATED

18

What to do with the answers?

"sampling system fouls too much"	"outputs for analytes a&b are too noisy for control"
"transitions from product D to E are problematic"	"there are too many analyzer outputs"
"model deployment S/W is not stable"	"output for analyte c is unstable at certain times"
"we really need a NEW method, for analyte z"	"instrument hardware is very hard to service"

Affinity diagram



Helps to focus on the REAL problems!

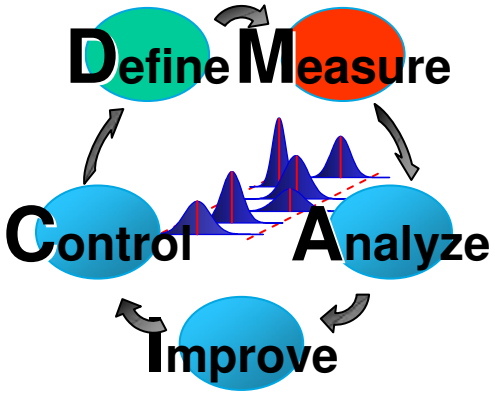
EIGENVECTOR RESEARCH INCORPORATED

19

EIGENVECTOR RESEARCH INCORPORATED

20

Measure: Measurement System Analysis



- Measure Phase:
  - Identify "The Project Y"
    - Ex. Effectiveness of Analyzer output "B"
  - Establish "baseline" performance
  - Assess, validate ***existing measurements***!
- Measurement System Analysis (MSA)
  - Is an existing measurement ***capable*** of assessing analyzer output quality?

EIGENVECTOR RESEARCH INCORPORATED

21

Measurement System Analysis

1. Identify ***all*** possible variation sources

Operator

Instrument ID Reagent supplier

2. Design and execute "variability experiment" on system

	Ref. Method Measurements	
Sample ID	Operator A	Operator B
1	2.650	2.698
2	2.096	2.115
3	3.033	3.015
4	2.712	2.698
5	2.111	2.125

3. Analyze data with appropriate tool (Gage R&R, ANOVA,..) to get measurement error, and contributions to error

Gage Error (GRR):	0.0987

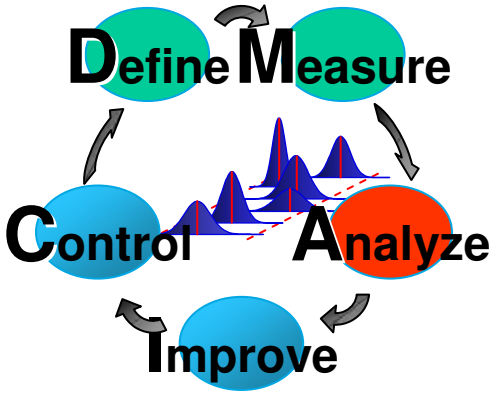
4. Compare error(s) to *Performance Specs*

Performance Spec (+/-)	2.000

EIGENVECTOR RESEARCH INCORPORATED

22

Analyze: Impact/Control

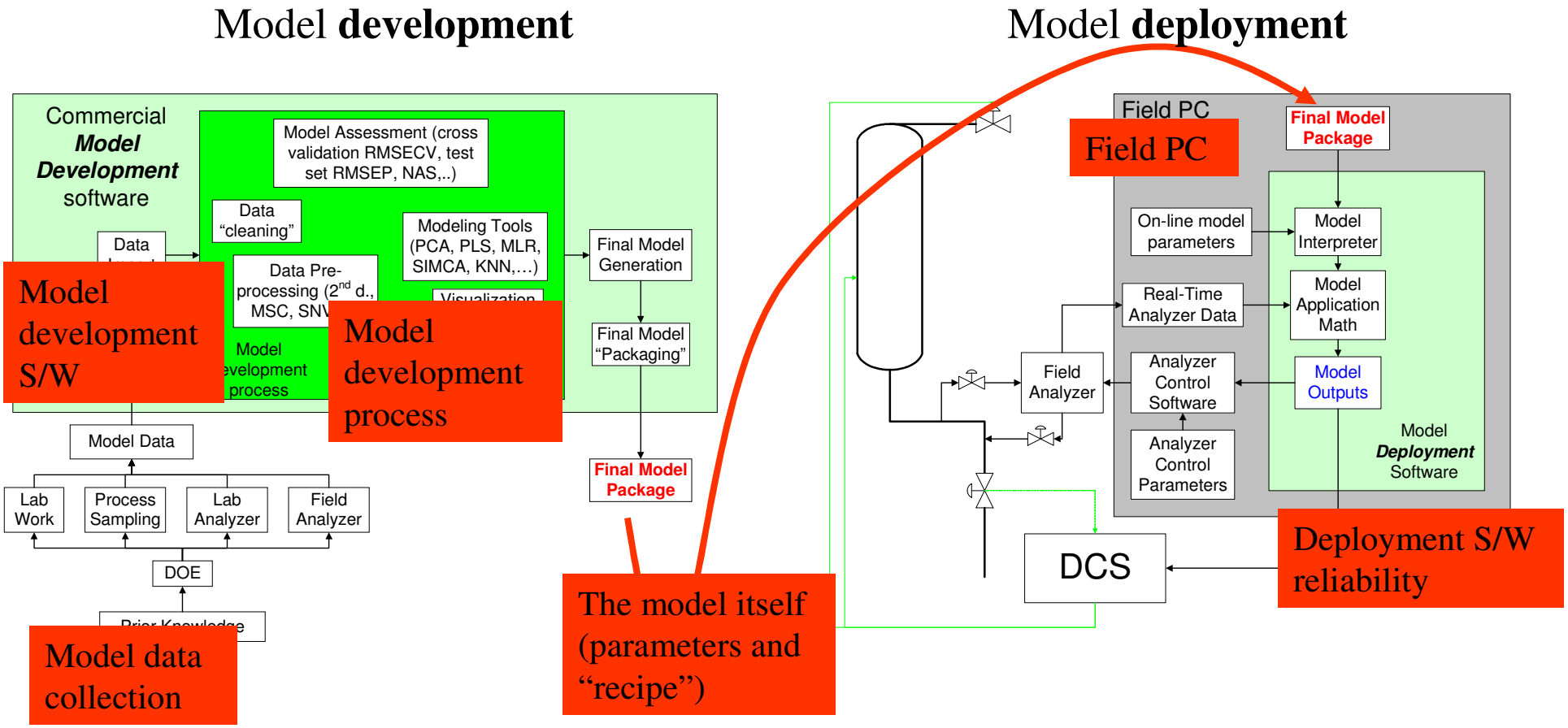


- Analyze Phase:
  - Identify ALL sources of variation in The Project Y (called "X"s)
  - Explore X/Y relationships
  - Start with many X's, reduce to a few critical X's
- Useful Tools
  - Cause and Effect ("fishbone", Ishikawa)
  - Process Map
  - Impact/Control Matrix

EIGENVECTOR RESEARCH INCORPORATED

23

Process Map

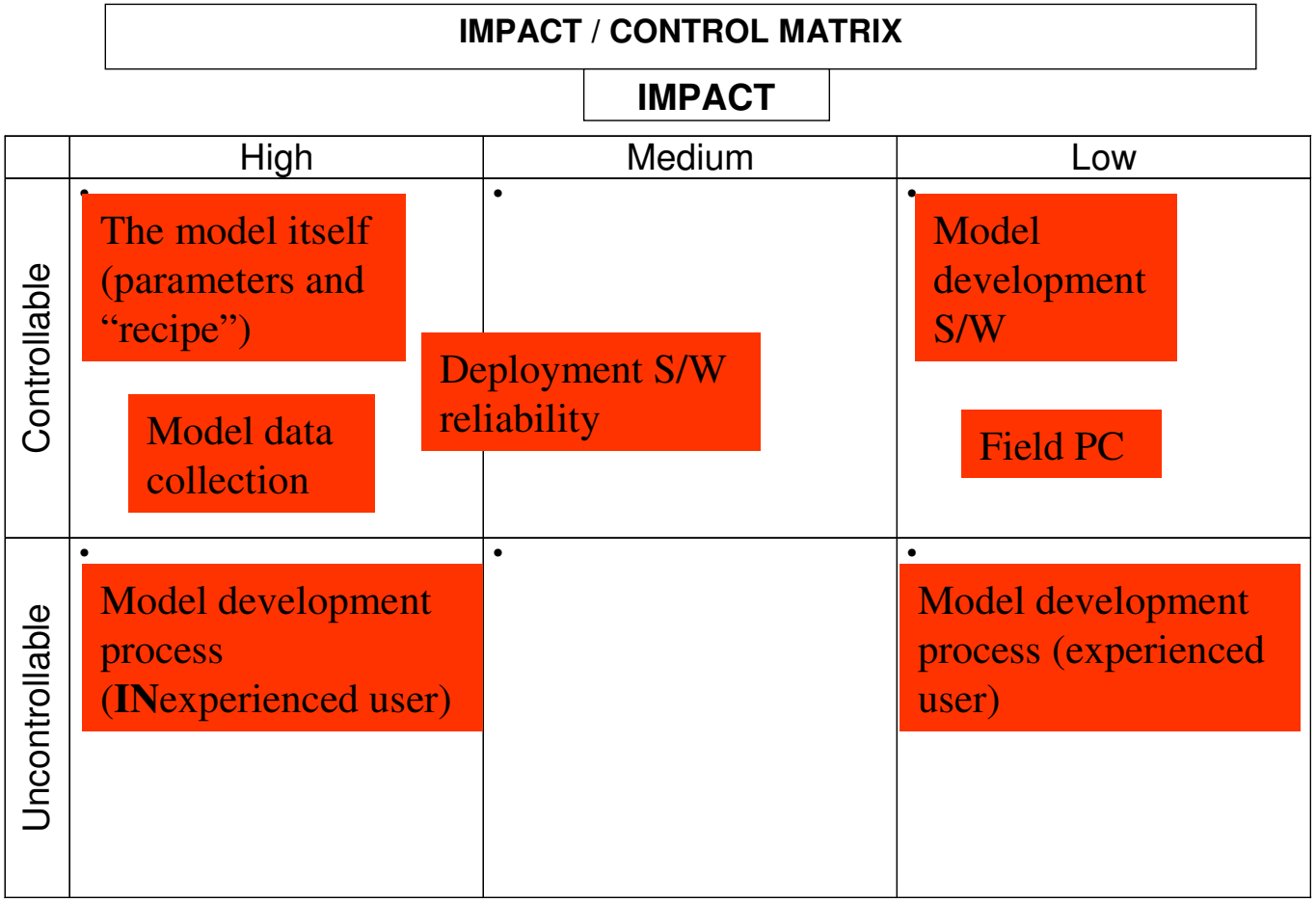


WHAT impacts analyzer effectiveness?

EIGENVECTOR RESEARCH INCORPORATED

24

Impact/Control Matrix



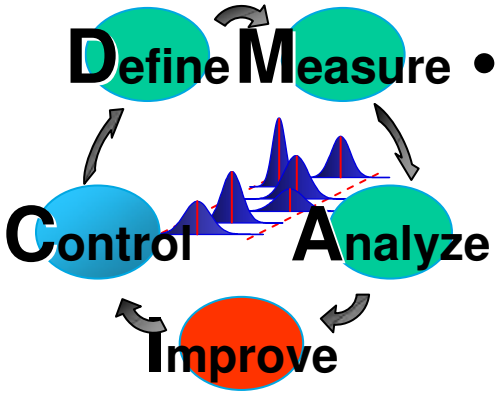
Focus on high impact and high controllability!

If high impact and low controllability- must address!

EIGENVECTOR RESEARCH INCORPORATED

25

Improve: Model Piloting

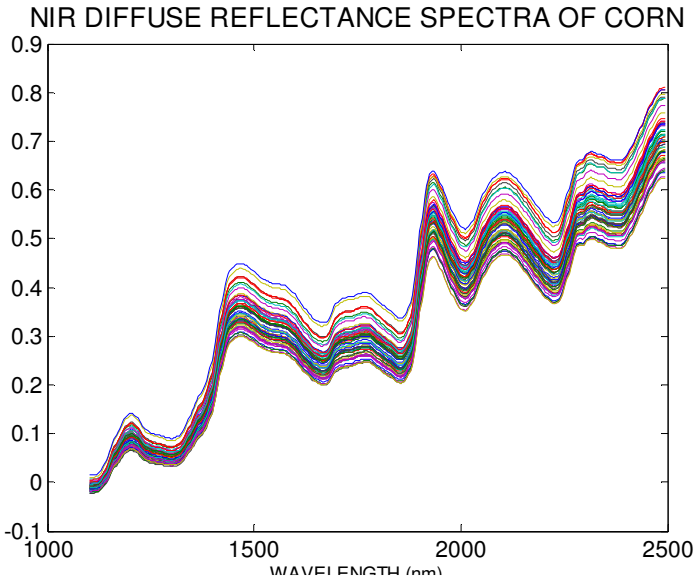


- Improve Phase:
  - Quantify changes needed to optimize improvement
  - Demonstrate that these changes will improve the process
  - What are tolerances in new settings?
- Useful Tools:
  - Risk assessment: FMEA!
  - Design of Experiments
  - Piloting the solution

EIGENVECTOR RESEARCH INCORPORATED

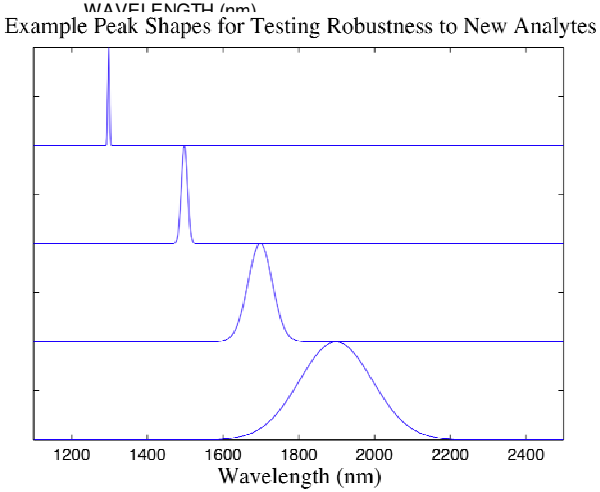
26

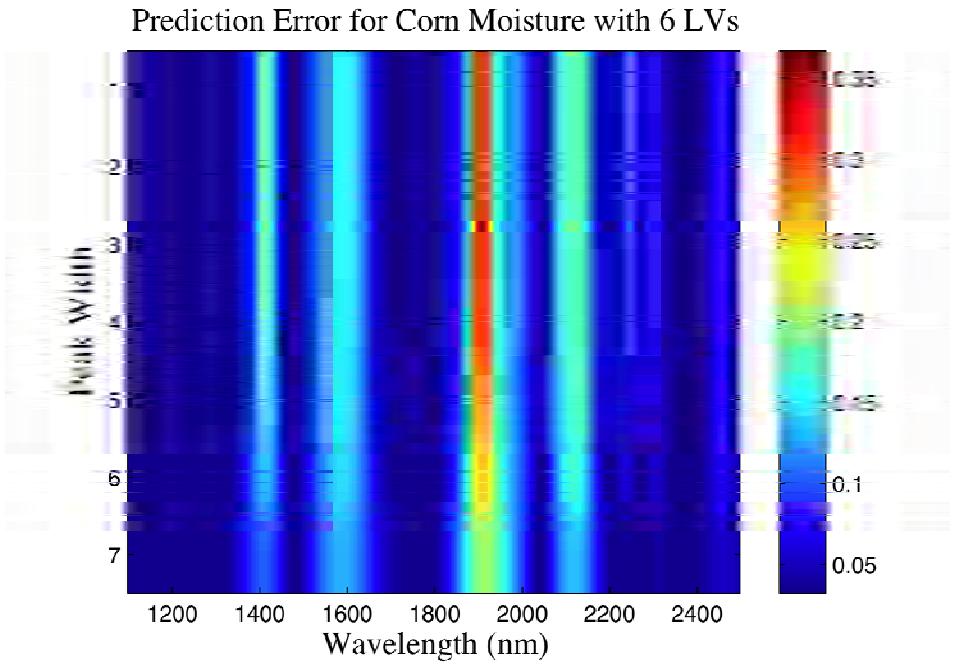
Model Piloting Tool



+ reference moisture data → MODEL (by BMW)

How affec addit comp



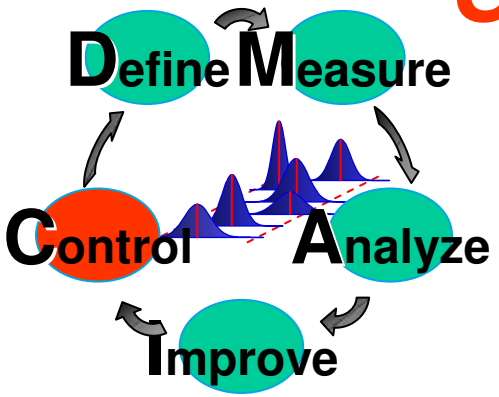


B. Wise, "Tools for Multivariate Calibration Robustness Testing with Observations on Effects of Data Preprocessing", CAC 2008

EIGENVECTOR RESEARCH INCORPORATED

27

Control: Control Plan



- Control Phase:
  - Implement "sustainable" solution
  - Assess REAL impact
  - Documentation, Translation
- Useful tools
  - Control charts
  - Control Plan: "lock in the gains"!

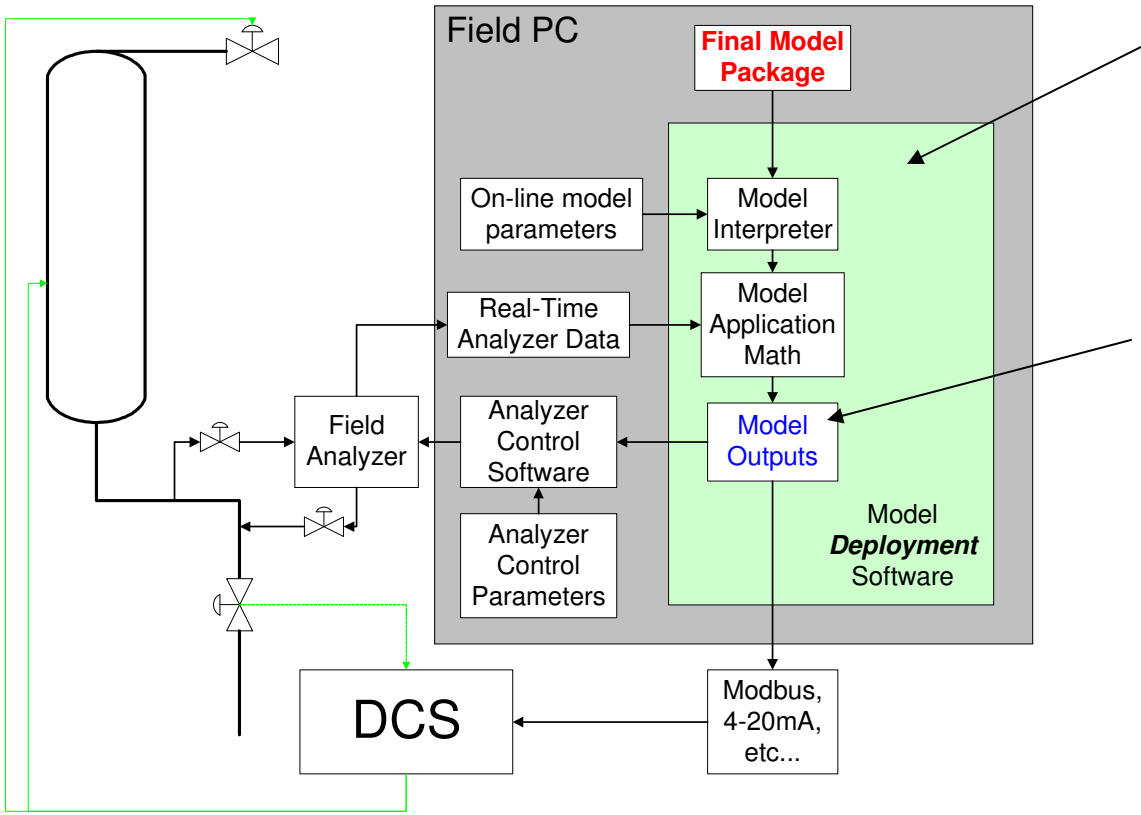
Dept. or Indiv.	Property	CTQ or X	Spec.	Meas. Tech.	Sample Size	Freq.	Who Measures	Where Recd.	Response Plan		
									Action	Timing	Owner

EIGENVECTOR RESEARCH INCORPORATED

28

Control Plan- PAT/Chemometrics

Quick model updating capability



Periodic auditing of DEPLOYMENT software

Monitor model performance: Hotelling's T2, Q Residuals

Remote Access (PCAnywhere/Timbuktu): Enabling Technology!

EIGENVECTOR RESEARCH INCORPORATED

29

Six Sigma Questionnaire

- Current & former DuPont colleagues
- Which element(s) of Six-Sigma do you feel were the most useful to your work?
- Did your "Six-Sigma experience" affect the way you operate?
- 8 respondents
  - 1 Master BB, 1 BB, 6 GB
  - 3 process analytical, 1 PAT management, 2 statisticians, process modeler, project engineer

EIGENVECTOR RESEARCH INCORPORATED

30

Questionnaire results

- Most useful elements:
  - Statistical toolset (3)
  - Voice of Customer tools (2)
  - Data-driven decision making (2)
  - Gage R&R (1)
  - Management Top-Down approach, “Bite-sized” projects, Documentation discipline, “Locking in” solutions, REAL validation of benefits, more data for process modeling
- Affect the way you operate?
  - 3 Yes: REAL value of new measurements, less “hard selling” of statistics!
  - 2 “Not Much” : Aware of tools already

31

Summary

- PAT, Chemometrics have much to contribute to Six Sigma, but..
- Six Sigma has much to contribute to PAT, Chemometrics

32

Acknowledgements

- Eigenvector Research Colleagues
- DuPont Colleagues
- DuPont Six Sigma

EIGENVECTOR RESEARCH INCORPORATED

33