

Pharmaceutical Quality System (ICH Q10) Conference
October 4-6, 2011 | Crystal Gateway Marriott | Arlington, Virginia
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Case Study: Use of Statistical Process Control to Detect Process Drift; Using Process Capability Measurement

Lynn Torbeck
Statistician

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Overview of Talk

- Define SQC, SPC
- State of control
- Process capability
 - Statistical Tolerance Intervals
 - Cpk
- Trending and drift
- Case Study

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Statistical Quality Control, SQC

- Specific statistical techniques used for end product quality control including data tabulation, probability, basic statistics, statistical sampling plans and reporting of defects, rejects and costs.

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Statistical Process Control, SPC

- Specific statistical techniques used to monitor, improve and control the manufacturing process itself. These include probability, basic statistics, statistical control charts, process capability studies and experimental design for improvement and optimization. Variability reduction is a major goal.

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Q10: "Establish and Maintain a State of Control"

- *A process can be in control for financial and accounting, for regulatory compliance, and for organizational and managerial control. These forms of control are usually assumed to be in place. There are two other states of control germane to our discussion of statistics.*

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Engineering Control

- *A process is said to be in a state of Engineering Control when the process can be changed and adjusted using control knobs and/or setting of the critical process parameters, (independent variables) that affect the dependent responses. The product always meets its specifications even if inconsistent and erratic. Time plots with specifications are used.*

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Statistical Control

- *A process is said to be in a state of Statistical Control when the process produces product that while containing variability in the critical quality attributes, (dependent variables), is predictable in that variability over time. Statistical control charts are used to monitor the process.*

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	In statistical control	Out of statistical control
In engineering control	Meets specifications and is statistically stable and predictable	Meets specifications for now but is not statistically stable or predictable
Out of engineering control	Statistically stable and predictable but exceeds specifications	Unacceptable process

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Process Capability

- *Process capability is measured by comparing the variability of the product/process to the width of the specification range. This is best done using Statistical Tolerance Intervals as they take into account the sample size where Cpk and Ppk do not. If Cpk is used then the lower confidence bound should be calculated and compared to the requirement*

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Statistical Tolerance Intervals

- A statement about the individual values
- Formula: $\text{Average} \pm K * \text{Std Dev}$
- The value for K depends on:
 - The sample size, n
 - The confidence level
 - The population percentage

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Cpk

- $C_{pu} = (\text{USL} - \text{Average}) / (3 * \text{Std Dev})$
- $C_{pl} = (\text{Average} - \text{LSL}) / (3 * \text{Std Dev})$
- $C_{pk} = \text{Minimum of } \{C_{pu} \text{ and } C_{pl}\}$
- If $C_{pk} \leq 1.0$, the process is not capable
- If $C_{pk} = 1.0$, the process is barely capable
- Suggest Cpk be greater than 1.33
- Suggest calculating the lower CI for Cpk

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Q10: Variability Reduction

- “Identify sources of variation affecting performance and product quality for potential continual improvement activity to reduce or control variation.”

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Q10: Variability Reduction

- *Six Sigma programs have gotten a poor reputation in some circles because of a single minded focus on saving money and not giving equal consideration to reducing variation and improving quality.*
- *Management needs to give equal attention and resources to both.*

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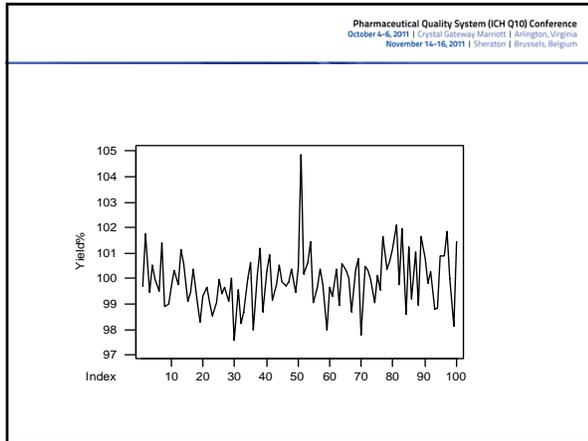
Trending and Process Drift

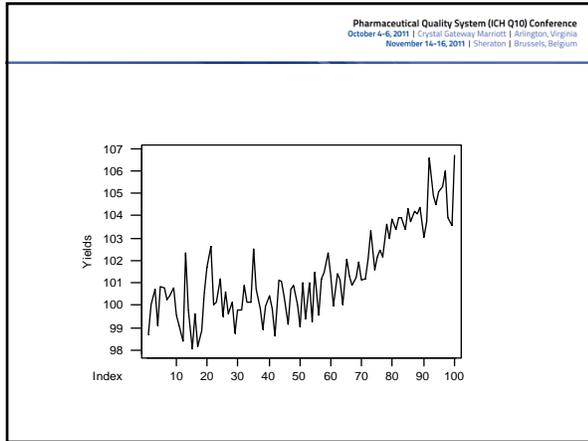
- Trending is the comparison of one or more reportable values collected over time versus a historical data set or a statistical model.
- Process drift has many definitions depending on the author.

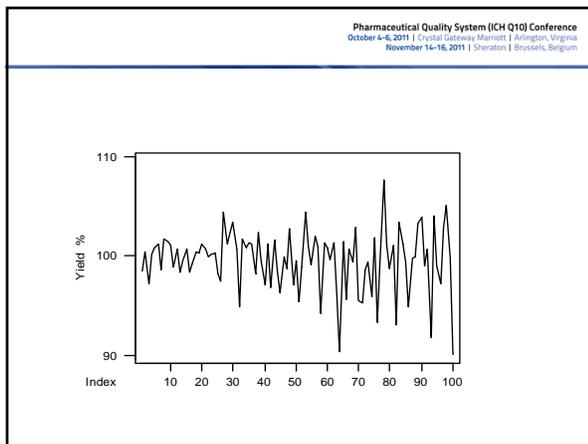
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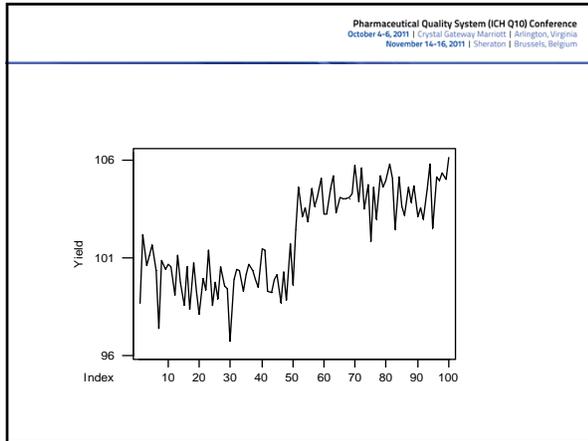
Five Out of Trend, OOT, Examples

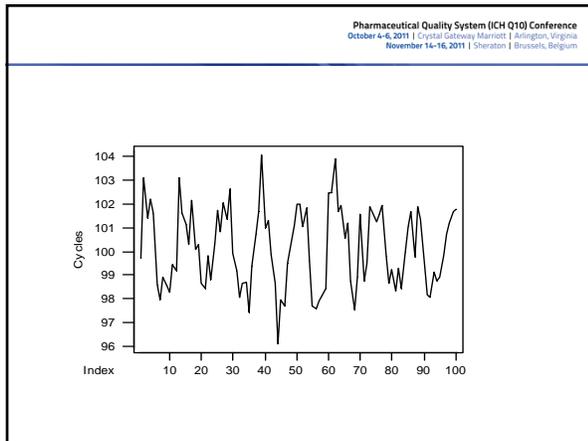
1. A single unusual value or outlier.
2. A change in the slope of the data or drift
3. A change in the variability
4. A shift in the average
5. Reoccurring cycles







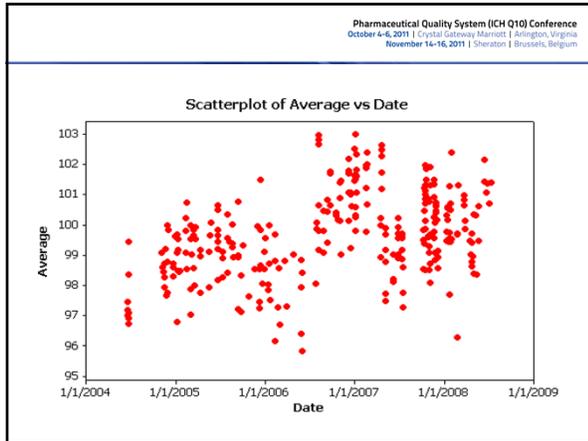


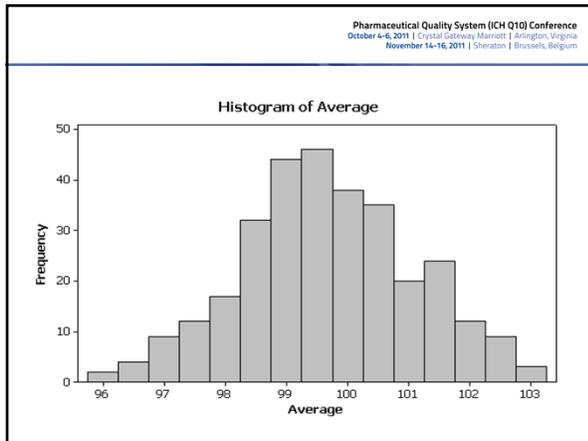


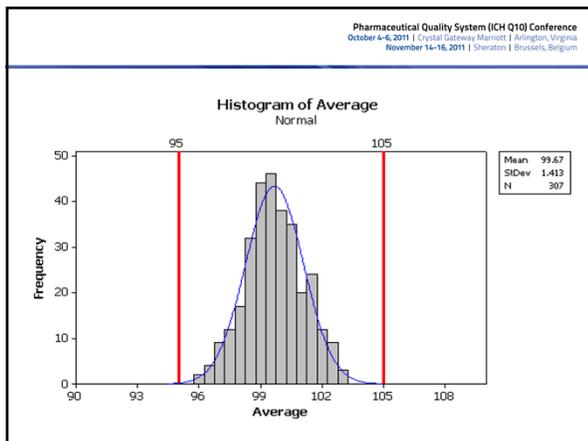
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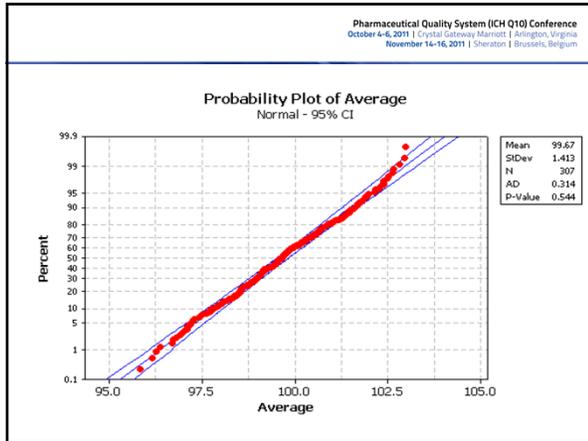
Case Study

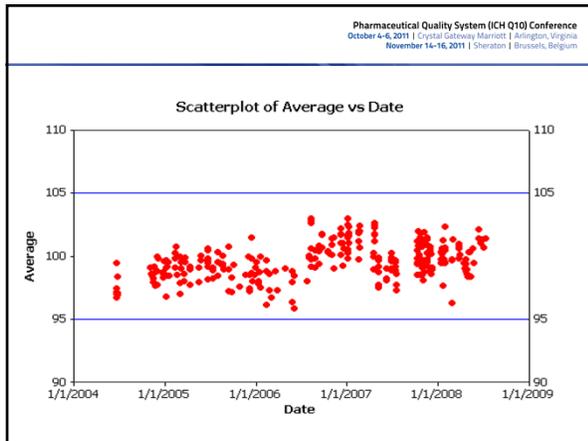
- 307 samples of size 6 have been collected
- The average has been found for groups of 6
- How do the data look trended over time?
- Plot the averages vs. date
- The graph is a Time Plot
- What observations can we make?

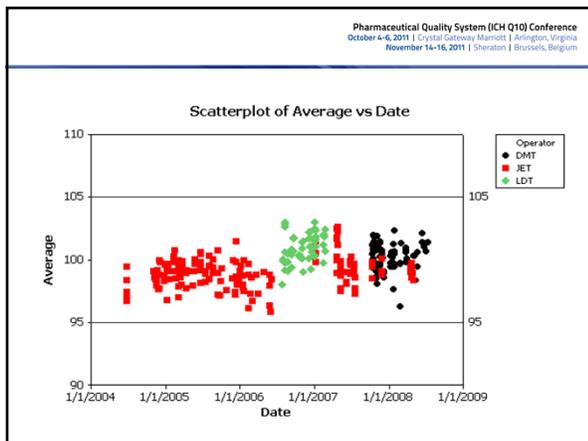


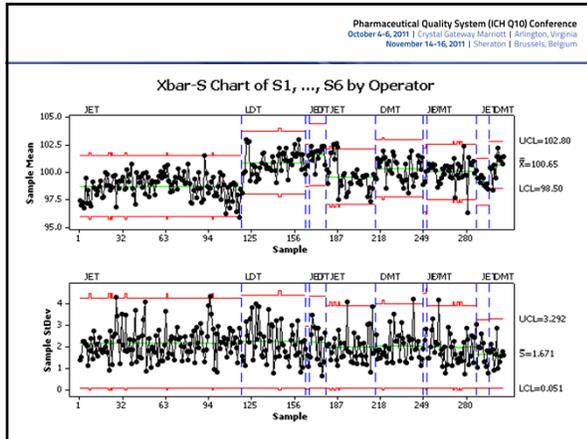












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Cpk

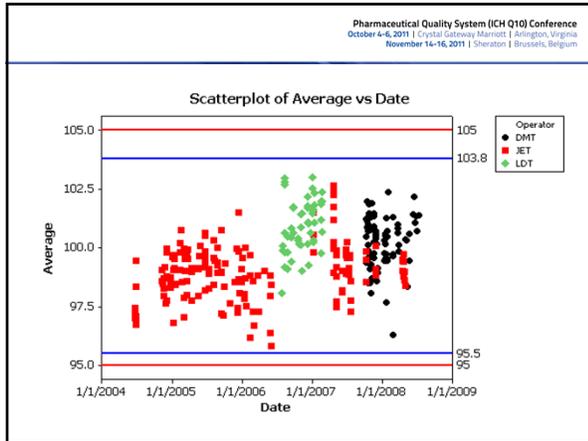
- $C_{pu} = (USL - \text{Average}) / (3 * \text{Std Dev})$
- $C_{pl} = (\text{Average} - LSL) / (3 * \text{Std Dev})$
- $C_{pk} = \text{Minimum of } \{C_{pu} \text{ and } C_{pl}\}$

- $C_{pu} = (105 - 99.68) / (3 * 1.413) = 1.3$
- $C_{pl} = (99.68 - 95.0) / (3 * 1.413) = 1.1$
- $C_{pk} = 1.1$

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- Formula: $\text{Average} \pm K * \text{Std Dev}$
- The value for K depends on:
 - The sample size, $n = 307$
 - The confidence level = 99%
 - The population percentage = 99%
- $K = 2.9225$ STI = 95.5% to 103.8%



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Case Study Recommendations

- The company should immediately begin a CAPA activity to find and correct the differences between operators.
- That should be followed by a project to reduce common cause variation and to center the process at 100.

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Conclusions

- This case study illustrates the use of simple statistical tools to study a process for control, capability, trending, and drift.
- Every quality unit and manufacturing unit should have staff trained and capable of this analysis on a routine basis.

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Thank You
