Pharmaceutical Quality Management

STATISTICAL QUALITY CONTROL

By:

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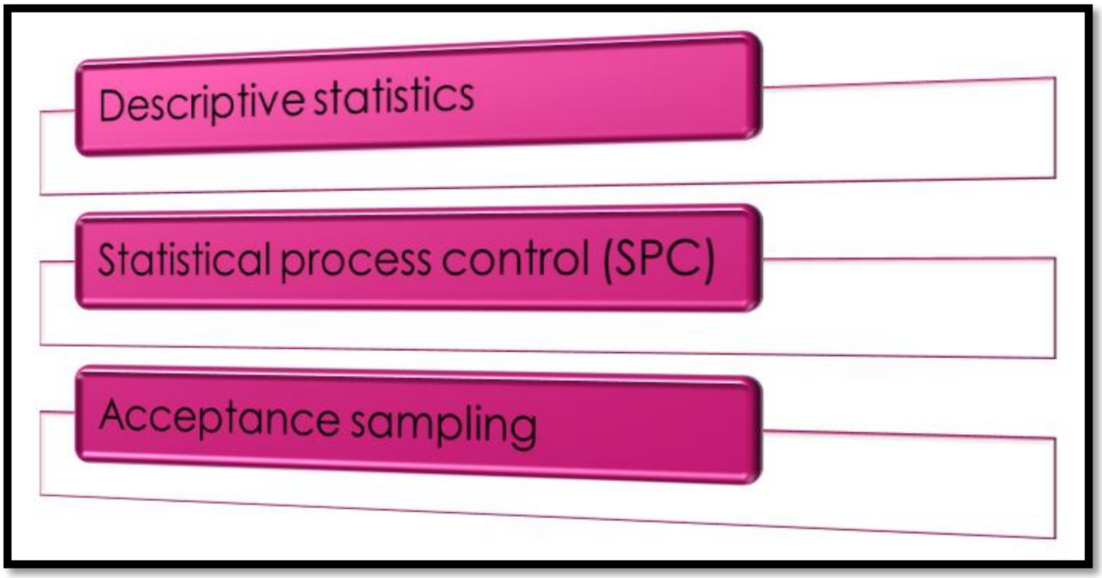
WHAT IS SQC?

Statistical quality control (SQC) *is the term used to describe the set of statistical tools used by quality professionals.*

- **SQC Categories**



1. DESCRIPTIVE STATISTICS

Descriptive statistics are used to describe quality characteristics and relationships.

a. **The Mean-** measure of central tendency
b. **The Range-** difference between largest/smallest observations in a set of data
c. **Standard Deviation** measures the amount of data dispersion around mean

a. The Mean

To compute the mean we simply sum all the observations and divide by the total no. of observations.

$$\bar{x} = \frac{\sum_{i=1}^{n} x_i}{n}$$

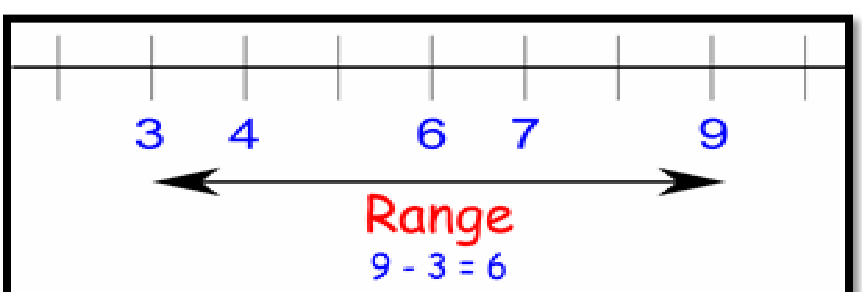
where $\bar{x}$ = the mean

x_i = observation i, $i = 1, \ldots, n$

n = number of observations

b. The Range:

Range, which is the difference between the largest and smallest observations



c. Standard Deviation

- *Standard deviation is a measure of dispersion of a curve.*
- *It measures the extent to which these values are scattered around the central mean.*

$$\sigma = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n - 1}}$$

where σ = standard deviation of a sample
$\bar{x}$ = the mean
x_i = observation i, $i = 1, \ldots, n$
n = the number of observations in the sample

2. STATISTICAL PROCESS CONTROL

- Extend the use of descriptive statistics to monitor the quality of the product and process
- Statistical process control help to determine the amount of variation
- To make sure the process is in a *state of control*

▶ **Variation in Quality**

- No two items are exactly alike.
- Some sort of variations in the two items is bound to be there. In fact it is an integral part of any manufacturing process.
- This difference in characteristics known as variation.
- This variation may be due to substandard quality of raw material, carelessness on the part of operator, fault in machinery system etc.

▶ Types Of Variations

A. Variation due to chance causes/common causes

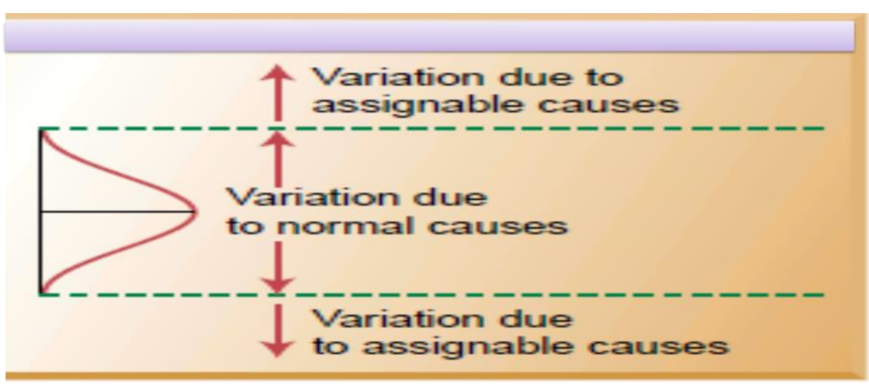
- Variation occurred due to chance.
- This variation is NOT due to defect in machine, Raw material or any other factors.
- Behave in "random manner".
- Negligible but Inevitable
- The process is said to be under the state of statistical control.

B. Variation due to assignable causes

Non – random causes like:

- Difference in quality of raw material
- Difference in machines
- Difference in operators

Difference of time



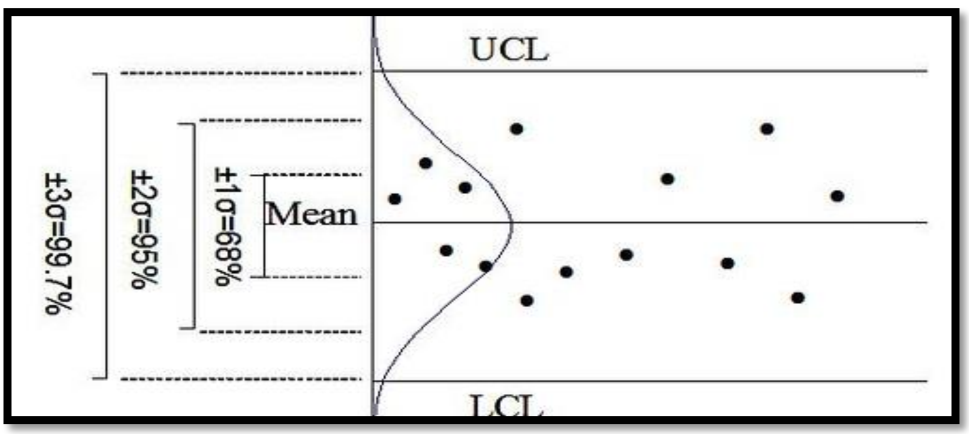
▶ Specification and control limits

- No item in the world can be a true copy of another item.
- It is not expressed in absolute values but in terms of a range.
- For Example:

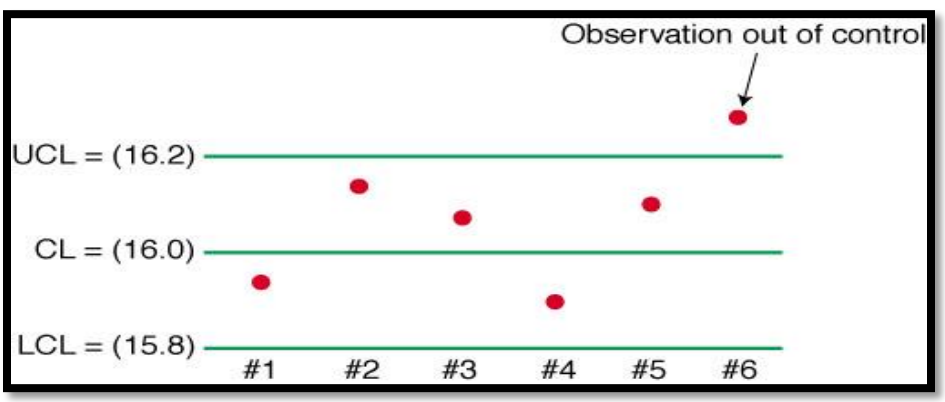
The diameter of a tablet punch is expected by its manufacturer not as 7mm but as 7mm ± 0.05.

Thus, the diameter of a tablet punch produced by the manufacturer can vary from 6.95 mm to 7.05 mm.

▶ Setting Control Limits



▶ HOW CONTROL LIMITS ARE USEFUL…..?



▶ SPC Methods-Control Charts

- Control Charts show sample data plotted on a graph with CL, UCL, and LCL
- Control chart for variables are used to monitor characteristics that can be measured, e.g. Hardness, weight, diameter, %age Assay
- Control charts for attributes are used to monitor characteristics that have discrete values and can be counted
- e.g. % age of Tables have mottling.

▶ Control Charts for Variables

a. x-bar charts

It is used to monitor the changes in the mean of a process (central tendencies).

b. R-bar charts

It is used to monitor the dispersion or variability of the process

Constructing a X-bar chart (sigma is not given)

- ▶ A factory produces 50 injections per hour. Samples of 10 injections are taken at random from the production at every hour and the amount of API of injection are measured (Assay). Draw X-bar and R charts and decide whether the process is under control or not.

Sample no.	x1	x2	x3	x4
1	230	238	242	250
2	220	230	218	242
3	222	232	236	240
4	250	240	230	225
5	228	242	235	225
6	248	222	220	230
7	232	232	242	242
8	236	234	235	237
9	231	248	251	271
10	220	222	224	231

Sample no.	x1	x2	x3	x4	Sigma Xi	Mean X-bar	Range R
1	230	238	242	250	960	240.00	20
2	220	230	218	242	910	227.50	24
3	222	232	236	240	930	232.50	18
4	250	240	230	225	945	236.25	25
5	228	242	235	225	930	232.50	17
6	248	222	220	230	920	230.00	28
7	232	232	242	242	948	237.00	10
8	236	234	235	237	942	235.50	3
9	231	248	251	271	1001	250.25	40
10	220	222	224	231	897	224.25	11
Total						2345.75	196

▶ <u>Calculation of x-bar and R-bar</u>

Now,

$$\bar{\bar{x}} = \frac{\sum \bar{x}}{m} = \frac{2345.75}{10} = 234.75$$

$$\overline{R} = \frac{\sum R}{m} = \frac{196}{10} = 19.6$$

Sample Size (n)	Factor for x-Chart A2	Factors for R-Chart D3	D4
2	1.88	0.00	3.27
3	1.02	0.00	2.57
4	0.73	0.00	2.28
5	0.58	0.00	2.11
6	0.48	0.00	2.00
7	0.42	0.08	1.92
8	0.37	0.14	1.86
9	0.34	0.18	1.82
10	0.31	0.22	1.78
11	0.29	0.26	1.74
12	0.27	0.28	1.72
13	0.25	0.31	1.69
14	0.24	0.33	1.67
15	0.22	0.35	1.65

(For n=4 A2= 0.73 D3= 0, D4=2.28)

▶ Control limits of X-Bar Chart:

- Central line C.L = $\overline{\overline{x}} = 234.75$
- U.C.L = $\overline{\overline{x}} + A2 \times \overline{R}$

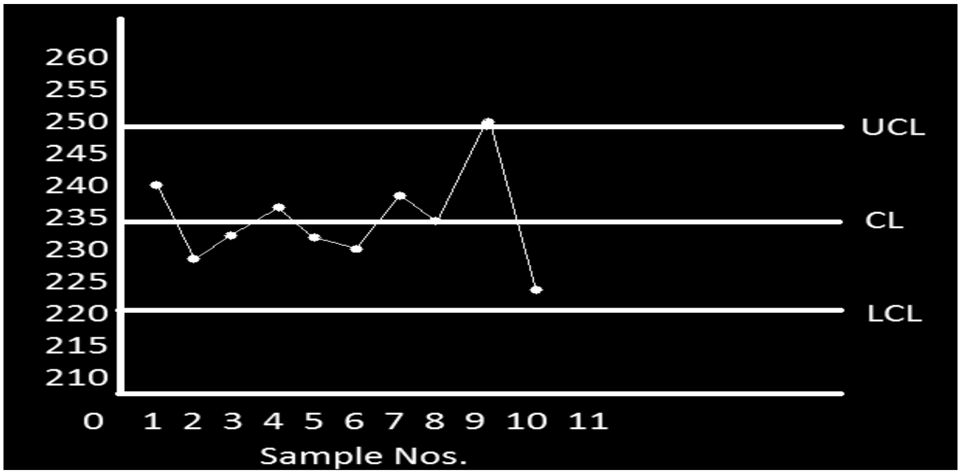
  =234.75 + (0.73) (19.6)

  =**249.06**
- L.C.L= $\overline{\overline{x}} - A2 \times \overline{R}$

  =234.75- (0.73) (19.6)

  =**220.72**

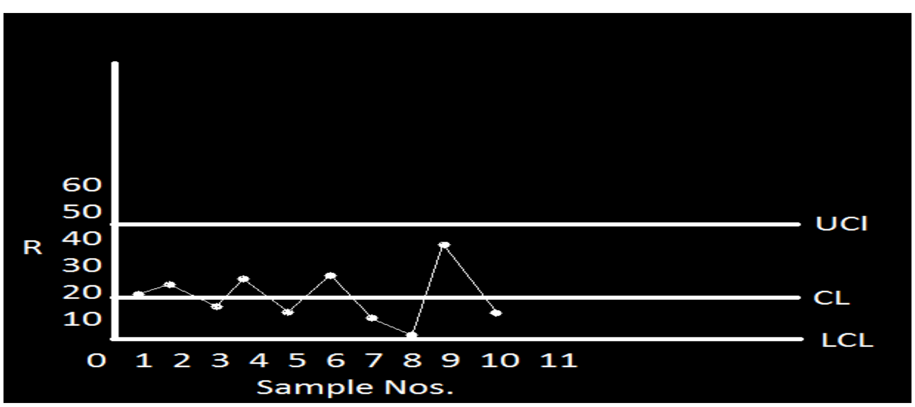
▶ **X-Bar Chart:**



▶ **Control limits of R-Bar Chart**

- Central Line = $\overline{R} = 19.6$
- U.C.L = $D4 \times \overline{R} = (2.28) \times (19.96)$
  =45.50
- L.C.L = $D3 \times \overline{R} = (0) \times (19.96)$
  =0

▶ **R-Bar Chart**



▶ <u>Control Charts for Attributes</u>

- Attributes are discrete events; yes/no, pass/fail

Use P-Charts for quality characteristics that are discrete and involve yes/no or good/bad decisions

- Number of leaking vials in a box of 48
- Number of broken syrup bottles in a carton

Use C-Charts for discrete defects when there can be more than one defect per unit

- Number of particulates in a vial sample taken from a production run
- Number of complaints per customer of pen injection insulin users

▶ <u>P-Chart Example</u>

A Production manager of a Pharmaceutical company has inspected the number of defective tablets in 20 random samples with 20 tablets in each sample. The table below shows the number of defective tablets in each sample of 20 tablets.

Calculate the control limits

Sample Number	Number of Defective Tires	Number of Observations Sampled	Fraction Defective
1	3	20	.15
2	2	20	.10
3	1	20	.05
4	2	20	.10
5	1	20	.05
6	3	20	.15
7	3	20	.15
8	2	20	.10
9	1	20	.05
10	2	20	.10
11	3	20	.15
12	2	20	.10
13	2	20	.10
14	1	20	.05
15	1	20	.05
16	2	20	.10
17	4	20	.20
18	3	20	.15
19	1	20	.05
20	1	20	.05
Total	40	400	

- **Solution**

The center line of the chart is

$$CL = \bar{p} = \frac{\text{total number of defective tires}}{\text{total number of observations}} = \frac{40}{400} = .10$$

$$\sigma_p = \sqrt{\frac{\bar{p}(1-\bar{p})}{n}} = \sqrt{\frac{(.10)(.90)}{20}} = .067$$

$$UCL = \bar{p} + z(\sigma_p) = .10 + 3(.067) = .301$$

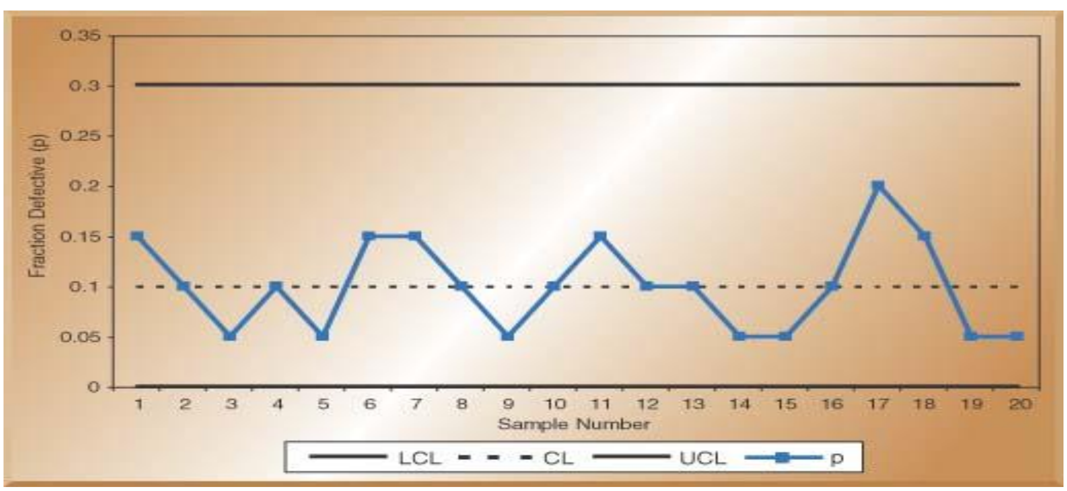
$$LCL = \bar{p} - z(\sigma_p) = .10 - 3(.067) = -.101 \longrightarrow 0$$

In this example the lower control limit is negative, which sometimes occurs because the computation is an approximation of the binomial distribution. When this occurs, the LCL is rounded up to zero because we cannot have a negative control limit.

▶ <u>Another Formula (simplified)</u>

$$\bar{p} \pm 3\sqrt{\frac{\bar{p}(1-\bar{p})}{n}}$$

▶ <u>P- Control Chart</u>



▶ C - Chart Example

The number of weekly customer complaints are monitored of pen injection insulin users using a c-chart. Develop three sigma control limits using the data table below.

— Number of weekly complaints are monitored. Complaints are recorded over twenty weeks

																					Tota
Week	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
No. of Complaints	3	2	3	1	3	3	2	1	3	1	3	4	2	1	1	1	3	2	2	3	44

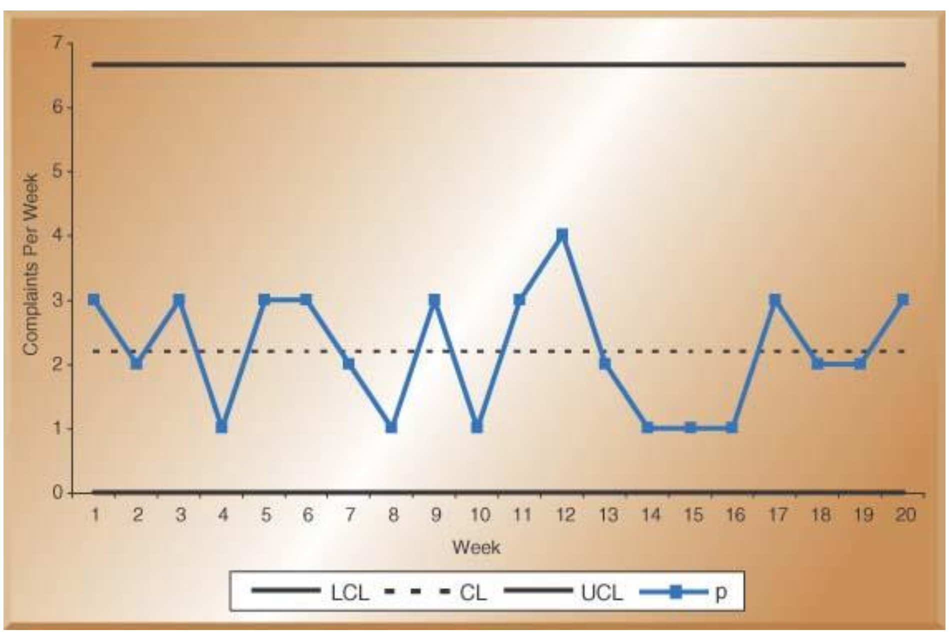
- **Solution**

The average number of complaints per week is $\frac{44}{20} = 2.2$. Therefore, $\bar{c} = 2.2$.

$$\text{UCL} = \bar{c} + z\sqrt{\bar{c}} = 2.2 + 3\sqrt{2.2} = 6.65$$
$$\text{LCL} = \bar{c} - z\sqrt{\bar{c}} = 2.2 - 3\sqrt{2.2} = -2.25 \longrightarrow 0$$

As in the previous example, the LCL is negative and should be rounded up to zero. Following is the control chart for this example:

▶ <u>C - Control Chart</u>



▶ Process Capability

- Evaluating the ability of a production process to meet or exceed preset specifications. This is called process capability.
- Product specifications, often called *tolerances*, are preset ranges of acceptable quality characteristics, such as product dimensions.

Two parts of process capability

- 1) Measure the variability of the output of a process, and
- 2) Compare that variability with a proposed specification or product tolerance.

1. Measuring Process Capability

To produce an acceptable product, the process must be *capable* and *in control* before production begins.

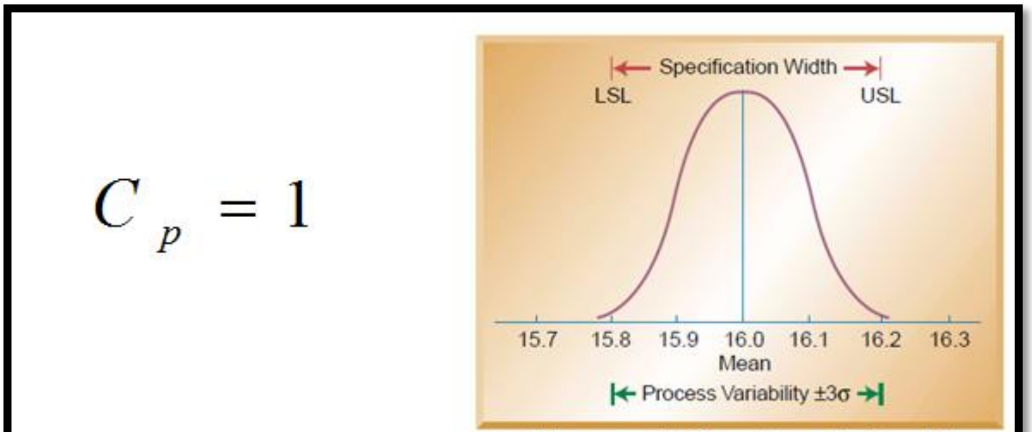
$$C_p = \frac{USL - LSL}{6\sigma}$$

Example

- Let’s say that the specification for the acceptable volume of Pharmaceutical liquid filled is preset at 16 ounces ±.2 ounces, which is 15.8 and 16.2 ounces.

Figure (a)

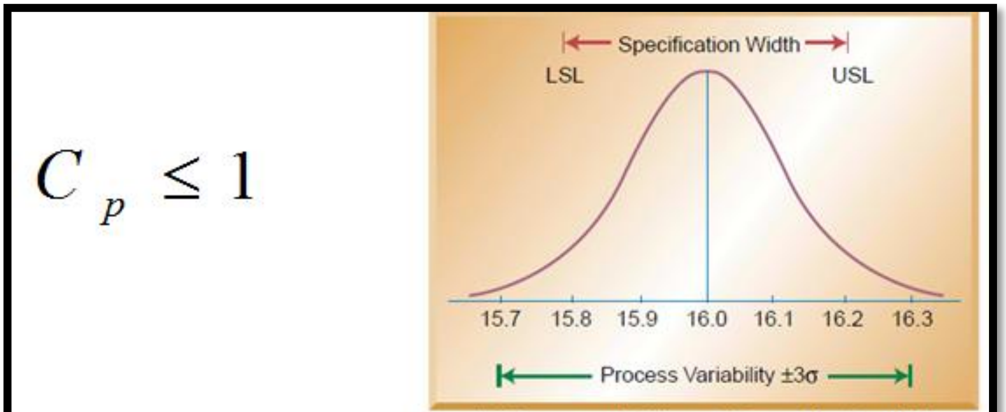
- The process produces 99.74 percent (three sigma) of the product with volumes between 15.8 and 16.2 ounces.



(a) Process variability meets specification width

Figure (b)

- The process produces 99.74 percent (three sigma) of the product with volumes between 15.7 and 16.3 ounces.

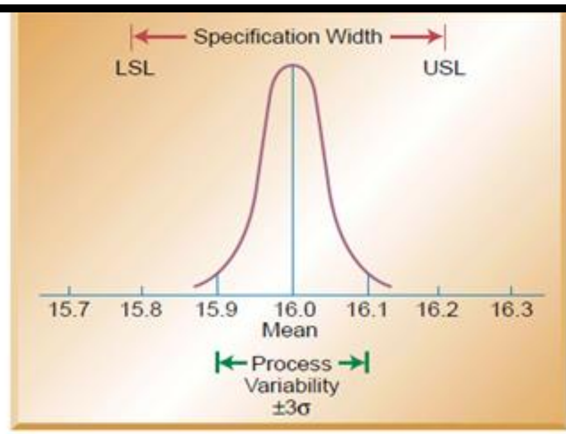


(b) Process variability outside specification width

Figure (c)

- The production process produces 99.74 percent (three sigma) of the product with volumes between 15.9 and 16.1 ounces.

$$C_p \geq 1$$



(c) Process variability within specification width