Basic Statistics and Pharmaceutical Statistical Applications

Second Edition

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plotting of the ranges. However, there appears to be a downward trend in the mean weights of the tablets and the operator should make adjustments in the process to return the weight back to the target mean.

Sometime **moving averages** and/or **moving ranges** are used for control charts. In these cases, the first two or three samples are averaged and the results used as the point on the control chart. When the next sample is collected, the first value is dropped and a new average is plotted (for both the mean and the range). This process continues, averaging including a new observation and excluding the earliest previous number continued for the whole data set. This yields a series of means and ranges represent the average of multiple consecutive data points.

A second type of control chart is the **cumulative sum** or **CUSUM** charting technique. It is considered more sensitive than Shewhart control charts to modest changes in the characteristic being monitored (Mason, 1989, p. 66). The CuSum charts are more effective in identifying gradual approaches to out-of-control conditions. The name CUSUM is from the fact that successive deviations are accumulated from a fixed reference point in the process. It provides a running, visual summation of deviations, from some preselected reference point. There is evidence of a special-cause variation when the cumulative sum of the deviations is extremely large or extremely small. Further information on CUSUM charts can be found in Mason's book (Mason, 1989, pp. 67-70).

Process Capability Indices

Process capability is a measure of the inherent variability of a process removing any undesirable special causes that might increase variability. It is the smallest variability due solely to common causes. In manufacturing it is a measurement of the degree to which the process is meeting the manufacturing requirements. It is the repeatability and consistency of that process and is relative to the customer requirements in terms of specification limits for the product.

Possible special causes of variability include different production sites, different equipment, and different operators running that equipment. One way to eliminate these special causes is to collect data using the same operator on the same machine, measuring the same batch of materials.

Studies of process capability are designed to determine what the process is "capable" of doing under controlled conditions (removing any special causes for variability). Another benefit of studying the process capability is to determine the stability of the process by comparing the output of a stable process with the process specifications or by comparing the normal variability of a stable process with the process specification limits.

Process capability compares the process outcome that is "in control" with the specification limits by measures called **capacity indices**. This comparison is a ratio of the deviation between the process specifications (called the specification width) to the deviation of the process values based on six process standard deviation units (referred to as the process width). A "capable process" is defined as one in which all the

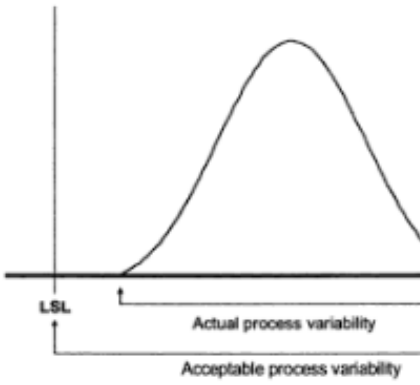

Figure 7.6 Illustration of a distribution within

Capability indices are equations employed to p
specific process in relationship to the product specifi
used to determine, given normal variation, if the p
established specifications. Thus, it is assumed that da
normally distributed population. Process capability is e
are three different indices, labeled C_p, C_{pk} and C_{pm}. The
only when there is a large sample size, usually a mini
should be consecutive data points, in at least 10
observations.

Several symbols are used in the calculations of t
target value for the product. The μ is the process m
dispersion based on historical experience with the proce
value). The *USL* and *LSL* are the upper and lower spe
The manufacture sets the specification limits. The speci
between the *USL* and *LSL*.

$$Specification\ range = USL$$

The specification range is usually from -3σ to $+3\sigma$, or
the previous chapter, approximately 99.7% of the are
would be within the plus or minus three sigmas. Thus,
in outcomes should have a total variation of approximat

C_p is a simple index that relates the acceptable v
limits to the natural variation of the process (expres

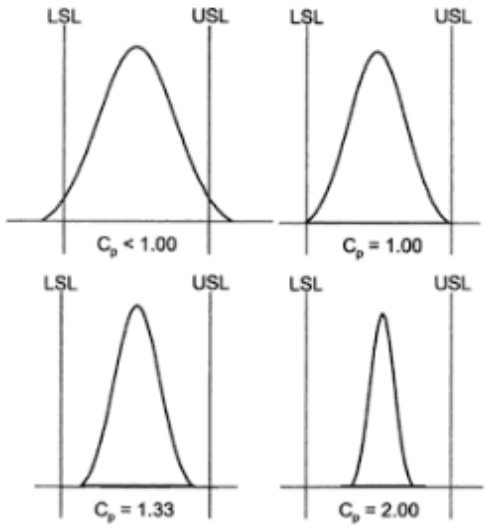

Figure 7.7 Distributions for various C_p values.

$$C_p = \frac{USL - LSL}{6\sigma} \qquad \text{Eq. 7.17}$$

Various C_p results are illustrated in Figure 7.7. If the C_p is less than one, the process variation exceeds specification, and a significant number of defects may be found. A C_p of less than one indicates that it is not a capable process; not capable of meeting specifications regardless of where the process mean is located. In these cases the process spread is greater than *USL-LSL*.

If the C_p equals one, the process is just meeting specifications and a minimum of 0.3% (100%-99.7%) defects will be detected if the process is centered at the target. This would be when a process is just barely capable; the process variability matches 6 σ. The C_p evaluates the spread of the process relative to the specification width, it does not provide information on how well the process average, μ, is centered with respect to the target value, T. If the process mean shifts slightly to the left or to the right, a significant amount of production output will exceed one of the two specification limits. In this case, the process must be watched closely to identify any shifts from the mean. Control charts are excellent for such monitoring.

If the C_p is greater than one, the process variation is less than the specification limits, but the defect rate might be greater if the process is not centered on the target

Table 7.4 C_p Values Assuming that the Center of the Distributi

USL–LSL	C_p	Rejects (parts per million)	%
6σ	1.000	2,700	
8σ	1.333	64	
10σ	1.667	0.6	
12σ	2.000	0.002	

value (T). Also, the C_p can be highly inaccurate and misle
sampled from a normally distributed population. Table 7.4
number of defects for various levels of C_p. As seen in Table 7.
more likely the process variability will fall within the specifica
less than *USL–LSL*). For example, with a C_p of 2.0 indicate
where 12 sigmas would fit between the USL and LSL. If a m
its specification limits, they might be able to claim that
consistent or uniform than their competitor. Some pharmaceu
establishing specific process capabilities targets. As a starting
a C_p of 1.33 for supplier qualifications and have a desired goal

A second process capability index is C_{pk} and comparing i
to get an indication of the difference between μ and T. T
follows:

$$C_{pk} = min\left[\frac{USL - \mu}{3\sigma}, \frac{\mu - LSL}{3\sigma}\right]$$

and the smaller of the two values (*min*) in the parentheses is re
process approaches a normal distribution and in statistical c
used to estimate the expected percent of defective products, sin

An alternative method for estimating the C_{pk} is:

$$C_{pk} = C_p(1-k)$$

where k is the scaled distance between the midpoint of the sp
the process mean, μ. This k-value comes from the Japanese
means deviation. The specification range is calculated as follo

$$m = \frac{USL + LSL}{2}$$

and the k value is derived using the equation