ASBC Methods of Analysis

Control Charting

Introduction

A typical question asked by brewers or other brewery personnel utilizing analytical laboratory data is, “how do I know that these results are accurate”? This question will most commonly be asked when the product or process results are out-of-specification. There are a number of potentially serious consequences for out of specification results including: (1) the need to retrieve product from the market, (2) disposing of product, and (3) potential fines for not meeting regulatory requirements. When asked to prove that the analytical data are correct, how do you respond?

There are a number of approaches to answer this question, but one statistical tool that can be utilized for internal quality control is control charting. A control chart is simply composed of individual or mean data plotted over time (1). A set of rules is applied to the data, and any result falling outside of the rules suggests that there is an issue with the measurement system.

This chapter on control charting laboratory data will provide an introduction to the topic. Options for more in-depth publications are listed in the reference section.

Normal Distribution

Control charts were originally developed by Shewart at Bell Laboratories as a tool around economic control of quality (2). If the assumption is made that the output data from an analytical instrument or a production process can be represented by a normal distribution, then either system can be monitored with control charts. Figure 1 represents a normal distribution with the mean (μ) and standard deviation (σ) values labeled.

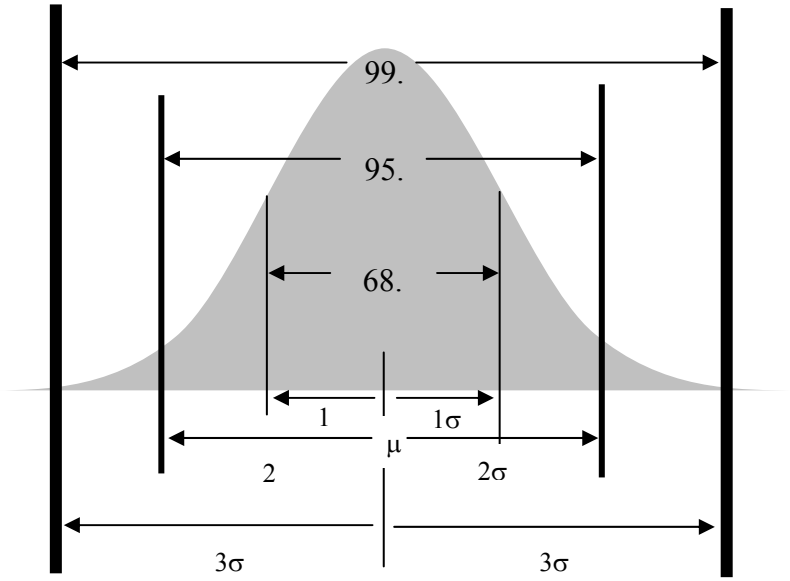


Figure 1 – Normal Distribution
(Figure adapted from a presentation given by Eric Samp to ASQ)

If the system is defined to be in control, 68.3% of the output results (assuming it will not change), will fall between +/- 1 σ, 95.5% of the results will fall within +/- 2 σ, and 99.7% of the output results will fall within +/- 3σ. From the IUPAC Harmonized Guidelines for Internal Quality Control in Analytical Chemistry Laboratories, two main categories of variation are recognized; random (common cause) and systematic (special cause) (3). Random error is based on the precision of the method (repeatability) and will fall on both sides of the mean. Systematic error is defined as the displacement of the mean of many determinations from the true value (3). Figure 2 illustrates the difference between random and systematic error.

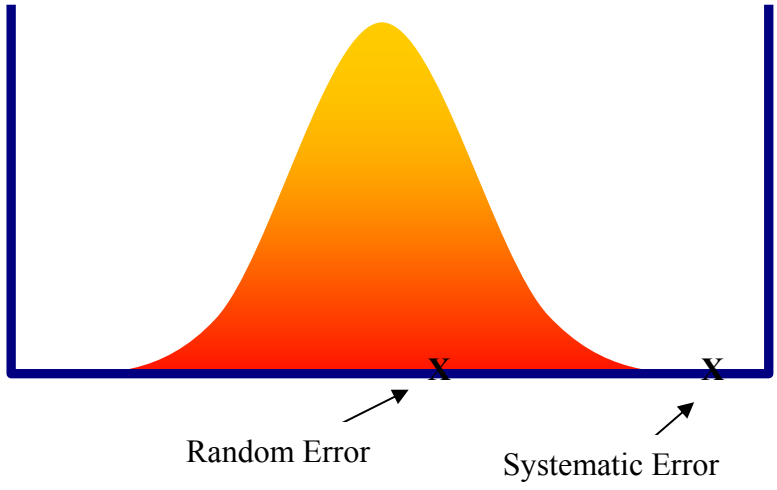


Figure 2 - Random and Systematic Error
(Figure adapted from a presentation given by Eric Samp to ASQ)

Examples resulting in systematic error that can be monitored by control charts are:

- Poor calibration
- Improper sample handling
- Mechanical issues with the instrumentation
- Contaminated/compromised samples

Control charts can be utilized both to determine if an analytical method is in control and as a routine monitor for the analytical method (4). When setting up control charts for routine monitoring, it is critical that the method be in control. If the method is in control, the data will follow the random statistical pattern demonstrated by the normal distribution.

Run and Range Charts

A number of control charts can be generated, but the simplest chart is the run chart (also known as the Shewhart or individual X chart). The run chart monitors the average of the measurement system. Figure 3 shows an example run chart for CO_2 analysis.

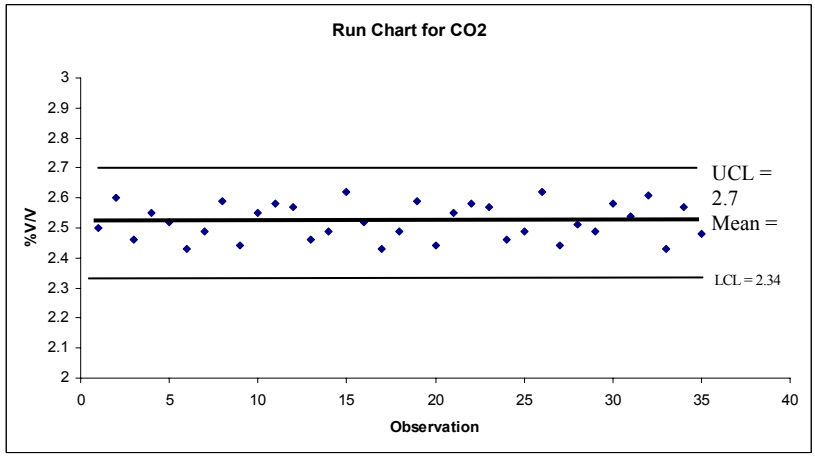


Figure 3 – CO_2 Run Chart

The x axis lists the observation number (an alternative is the date or time plotted on the x-axis) and the y axis lists the CO_2 result for the observation.

The chart lists the mean value or center line (CL) of the control sample (control samples will be covered in more detail in a later section) and the control limits. The center line is calculated using Equation 1, the upper control limit (UCL) is calculated using Equation 2, and the lower control limit (LCL) is calculated using Equation 3.

$$CL_{IX} = \overline{X}$$

Equation 1 – Control Limit Calculation
($\overline{X}$ is the total divided by the # of data points)

$$UCL_{IX} = \overline{X} + 3 \times \left[\frac{\overline{MR}}{1.128} \right]$$

Equation 2 – Upper Control Limit Calculation
($\overline{MR}$ = the average of the magnitudes of the differences between successive plotted points)

$$LCL_{IX} = \overline{X} - 3 \times \left[\frac{\overline{MR}}{1.128} \right]$$

Equation 3 – Lower Control Limit Calculation
($\overline{MR}$ = the average of the magnitudes of the differences between successive plotted points)

A number of rules can be applied to control charts to identify results that are out of statistical control indicating that systematic error is present. Four common rules are (4):
1) Any point outside of +/-3 standard deviations (s) (UCL from Equation 2 and LCL from Equation 3). For a system in control, only 3 out of 1000 points will fall outside of this range due to random error.
2) A run of 8 points all above or below the mean (center line). For a system in control, the probability that this will occur due to random error is $(1/2)^8 = 1/256$.
3) Eight consecutive points running upward or downward.
4) Any non-random patterns (identified by the analyst).

Additional rules can include (1):
1) Fourteen consecutive points alternating between up and down.
2) Two out of 3 consecutive points above the warning limits (warning limits are +/- 2s).
3) Four out of five consecutive points beyond 1s.

In determining how many rules to apply to the chart, more is not always better. As the number of rules that are applied is increased, the false alarm rate will increase (i.e. concluding that a change has occurred when in reality it has not).

Run charts are useful for monitoring a shift in the analytical method (such as a bias in the calibration). Moving Range (MR) charts can be used to monitor the method repeatability (such as a change in the consistency of an internal standard addition). A sample MR range chart for the same CO_2 data used in Figure 3 is shown in Figure 4.

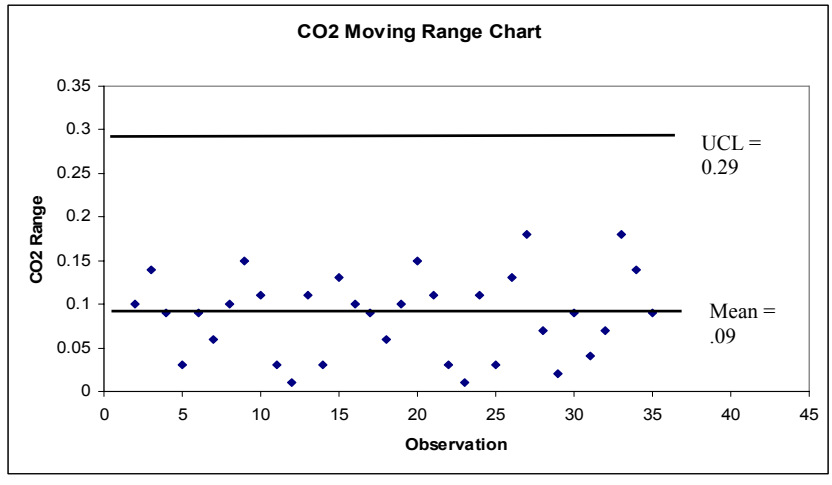


Figure 4 – CO_2 Moving Range Chart

The MR range chart plots the difference between sample points in chronological order on the y-axis and the x-axis lists the observation (or date/time). The center line is determined by calculating the average of the moving ranges. The control limits are calculated differently and require the use of a statistical table (Table 2). Equation 4 is the formula for calculating the lower control limit and Equation 5 is the formula for calculating the upper control limit.

$$LCL = \overline{MR} \times D_3$$

Equation 4 – Lower Control Limit Calculation for Range Chart
($\overline{MR}$ = the average of the magnitudes of the differences between successive plotted points and D_3 is from Table 2)

$$UCL = \overline{MR} \times D_4$$

Equation 5 – Upper Control Limit Calculation for Range Chart
($\overline{MR}$ = the average of the magnitudes of the differences between successive plotted points and D_4 is from Table 2)

Table 1 lists the data used to tabulate both the run and range charts. As an example for calculating the individual range values, the difference between observation 2 and observation 3 is 0.14. If you average the difference between each of the observations, the value is 0.09 (MR), which is shown on Figure 4. The UCL was calculated by multiplying the moving range mean times D_4 for n=2 observations from Table 2 (0.09 * 3.267 = .029). For the LCL the moving range mean was multiplied by D_3 for n = 2 observations from Table 2 (0.09 * 0 = 0).

Table 1 – Data Used for Calculating CO_2 Run and Range Charts

Observation	CO_2 Result	Difference
1	2.5	
2	2.6	0.1
3	2.46	0.14
4	2.55	0.09
5	2.52	0.03
6	2.43	0.09
7	2.49	0.06
8	2.59	0.1
9	2.44	0.15
10	2.55	0.11
11	2.58	0.03
12	2.57	0.01
13	2.46	0.11
14	2.49	0.03
15	2.62	0.13
16	2.52	0.1
17	2.43	0.09
18	2.49	0.06
19	2.59	0.1
20	2.44	0.15
21	2.55	0.11
22	2.58	0.03

23	2.57	0.01
24	2.46	0.11
25	2.49	0.03
26	2.62	0.13
27	2.44	0.18
28	2.51	0.07
29	2.49	0.02
30	2.58	0.09
31	2.54	0.04
32	2.61	0.07
33	2.43	0.18
34	2.57	0.14
35	2.48	0.09
Average	2.521	0.09
Standard Deviation	0.061	

Table 2 – Statistical Parameters for Calculating Control Limits for Range Charts

n	D_3	D_4
2	0	3.267
3	0	2.574
4	0	2.282
5	0	2.114
6	0	2.004
7	0.076	1.924
8	0.136	1.864
9	0.184	1.816
10	0.223	1.777

Control Sample Setup and Frequency

A number of options exist for the preparation of control samples (3). One option is to purchase a reference material with a known value. The known value would then be used as the center line in the control chart. The advantage to using a reference material is the center line is already known and the concentration(s) could be set close to the value typically observed from samples run in the lab. The disadvantages are cost (this can be very expensive) and the material will most likely not be a perfect match to the sample matrix. A second option is to create or formulate a control with

a known value. This has a similar set of advantages and disadvantages to the first option, but it could be created to be a better match to the sample matrix. The third option is to use a sample measured in a proficiency scheme (do you want to define this in sl more detail?). The center line would then be set to the mean value obtained in the proficiency testing. There is less control over the sample concentration with this option and the cost may be high. The advantage is that the sample should be a good matrix match and the mean value should be well established through testing in multiple laboratories by potentially a number of different methods. The forth option is to use a routine production sample (that is stable or can be stabilized) and assign the mean value through testing. A general rule is that a minimum of 30 replicates should be run to establish the mean value. This has the advantage of matching the matrix, it is inexpensive, and it should be close to the standard analyte concentration. The disadvantages are that the true value is not known and work is required to establish the mean value.
In general, the following should be considered when establishing a control sample:

1) What is the stability of the control sample? Will it last an adequate amount of time to be useful as a control?
2) Is the matrix similar or equivalent to the routine samples?
3) Is the concentration representative of routine sample concentrations?
4) What are the cost considerations?

From the IUPAC Harmonized Guidelines for Internal Quality Control in Analytical Chemistry Laboratories, recommendations have been set for the frequency of control sample analysis (3).

1) *Short (e.g., n<20) frequent runs of similar material.* Here the concentration range of the analyte in the run is relatively small, so a common value of standard deviation can be assumed. Insert a control material at least once per run. Plot either the individual value obtained, or the mean value, on an appropriate control chart. Analyze in duplicate at least half of the test materials, selected at random. Insert at least one blank determination.

2) *Longer (e.g., n>20) frequent runs of similar materials.* Again a common level of standard deviation is assumed. Insert the control material at an approximate frequency of one per ten test materials. If the run size is likely to vary from run to run, it is easier to standardize on a fixed number of insertions per run and plot the mean value on a control chart of means. Otherwise plot individual values. Analyze in duplicate a minimum of five test materials selected at random. Insert one blank determination per ten test materials.

3) *Frequent runs containing similar materials but with a wide range of analyte concentration.* Here we cannot assume that a single value of the standard deviation is applicable. Insert control materials in total numbers approximately as recommended above. However, there should be at least two levels of analyte represented, one close to the median level of typical test materials (do you mean ‘samples’?), and the other approximately at the upper or lower decile, as appropriate. Enter the values for the two control materials on separate control charts. Duplicate a minimum of five test materials, and insert one procedural blank per ten test materials.

4) *Ad hoc analysis.* Here the concept of statistical control is not applicable. It is assumed, however, that the materials in the run are of a single type, i.e., sufficiently similar for general conclusions on error to be made. Carry out duplicate analysis on all of the test materials. Carry out spiking or recovery tests or use a formulated control material, with an appropriate number of insertions (see above), and with different concentrations of analyte, if appropriate. Carry out blank determinations. As no control limits are available, compare the bias and precision with fitness–for-purpose limits or other established criteria.

The guidelines listed above are in depth, but as a simple summary: Analyze a minimum of 1 control sample for short runs. For longer runs, utilize 1 control sample for every 10 samples with control samples also used at the beginning and end of each run.

Control Chart Options

The options for setting up control charts are numerous. When considering what tool to use to produce the charts, the following should be considered:
1) Ease of use.
2) Cost.
3) Automation (taking data directly from the instrument into the software)
4) Complexity of control charts (what rules are going to be applied)
5) Additional statistical functions available in the software.

The most basic solution for setting up control charts is a pencil, graph paper, calculator and ruler. The next level would be using a simple software program such as Excel to manually setup the charts. There are also a number of Excel add-ons available to automate the charts. More complex statistical software includes Minitab®, Northwest Analytical, and InfinityQS®. A number of additional software packages exist and new options frequently become available. Do not consider the list above to be complete or as an endorsement for any particular option.

References

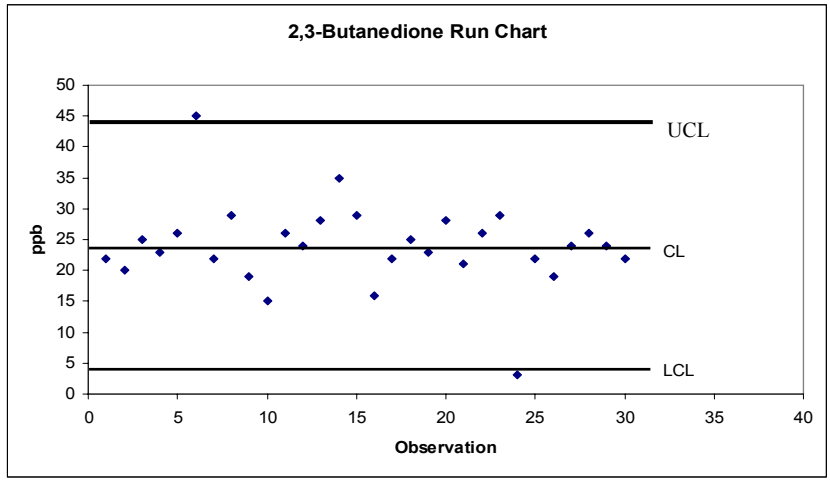
1) Triola, M.F. Elementary Statistics Using Excel, 3rd ed. Pearson Education: Boston (2007).
2) Shewhart, W.A. Economic Control of the Quality of Manufactured Products, Macmillan: London (1931).
3) Harmonized Guidelines for Internal Quality Control in Analytical Chemistry. Pure & Appl. Chem. 67(4):649 (1995).
4) Mullins, E. Statistics for the Quality Control Chemistry Laboratory. The Royal Society of Chemistry: Cambridge (2003).

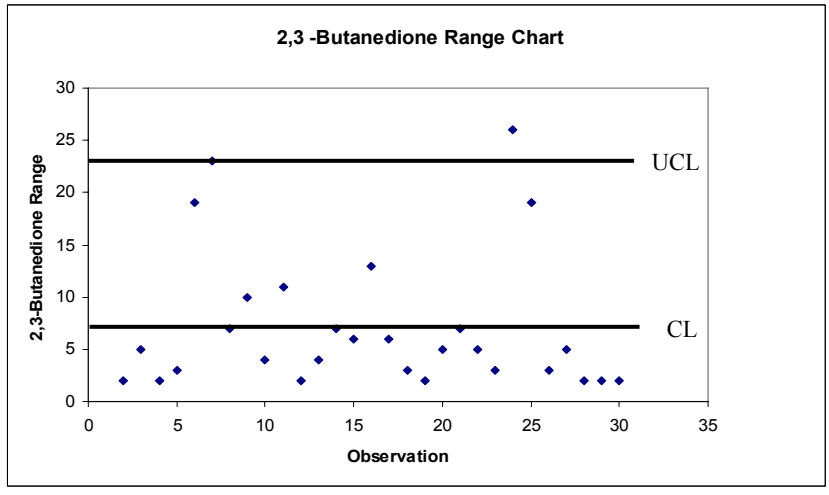
See next pages for examples.
Click here to go to the Control Charting Worksheets

Examples

Example 1

Control limits are being generated for a Gas Chromatographic method to measure 2, 3-butanedione. An end-of-fermentation sample was used as a control and the sample was analyzed 30 times (full preparation, different technicians, different days, etc.). The samples were centrifuged to remove yeast and frozen to maintain sample stability. The results were plotted on the run and moving range charts below to establish the control limits.



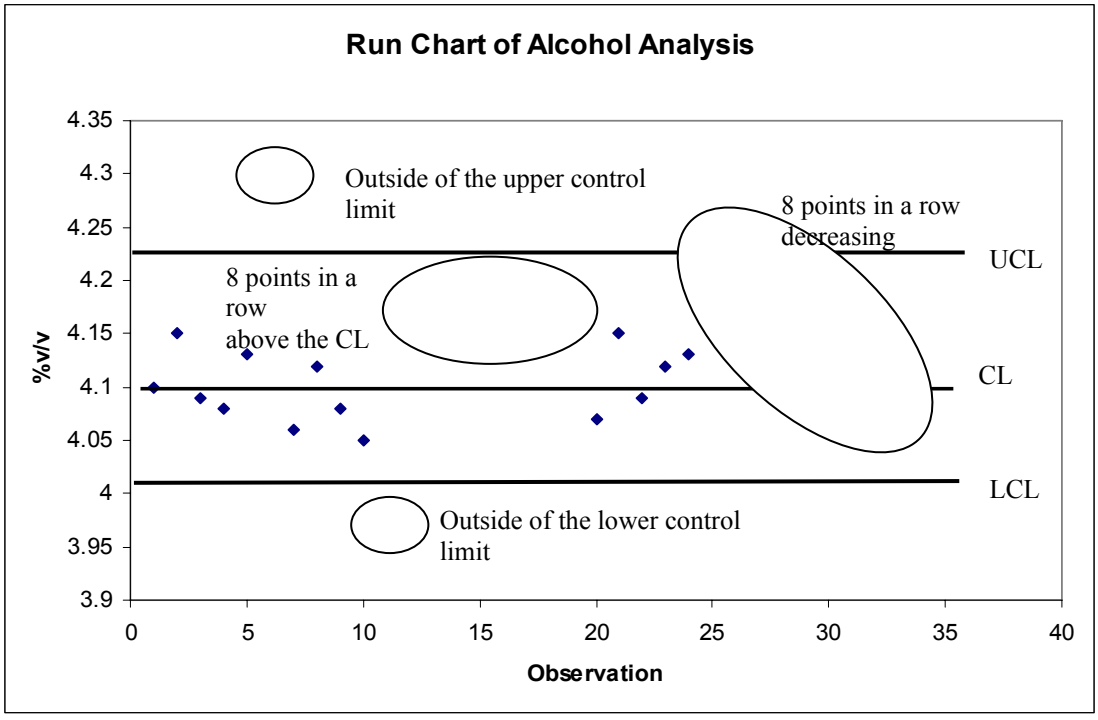


Analysis: The run and range charts both have points outside of the control limits. With the large spread in the data and data outside of the control limits, the center line and control limits will not provide meaningful guidelines for monitoring routine data. The method is not in control and corrective action should be taken prior to establishing routine control charts. In addition to multiple points that are out of the control limits, the spread in data is far greater than what would be expected for the analysis of 2, 3-butandione by GC. The method would not be an adequate tool to be used for monitoring the production process.

Observation	2,3-Butanedione (ppb)	Difference
1	22	
2	20	2
3	25	5
4	23	2
5	26	3
6	45	19
7	22	23
8	29	7
9	19	10
10	15	4
11	26	11
12	24	2
13	28	4
14	35	7
15	29	6
16	16	13
17	22	6
18	25	3
19	23	2
20	28	5
21	21	7
22	26	5
23	29	3
24	3	26
25	22	19
26	19	3
27	24	5
28	26	2
29	24	2
30	22	2

Example 2

Control limits were established for a method to measure alcohol in packaged beer. The method was determined to be in control and routine control run data are plotted below. Four of the rules were violated and are labeled on the chart below. It is recommended to note on control charts what corrective actions were taken for results breaking the control chart rules. For example, for the 8 points above the center line it could be noted that this was a bad calibration and that all of the data was re-analyzed. The advantages to keeping the notes directly on the charts are the next analyst will know that action was taken and it is a historical record to note what was done to correct the problem.

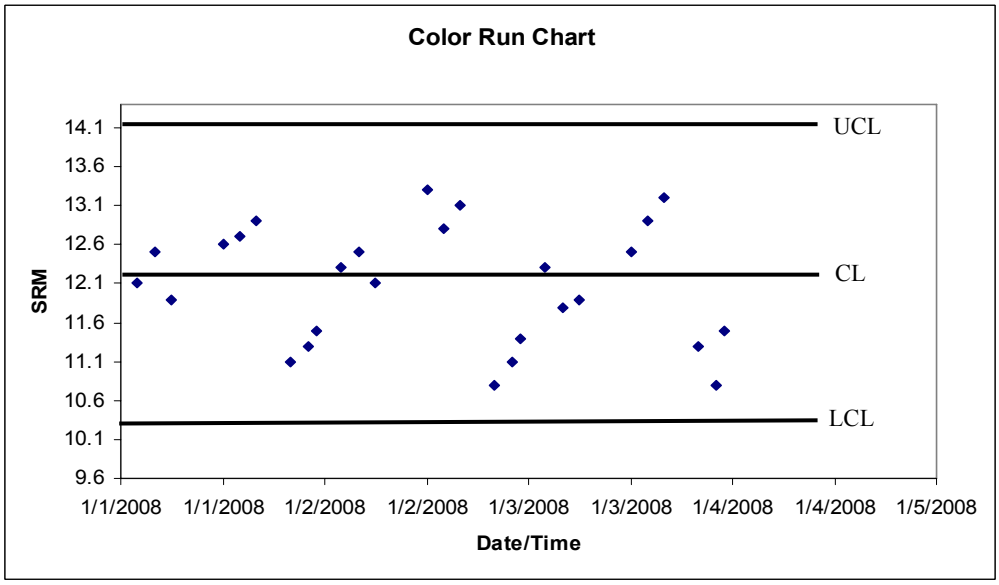


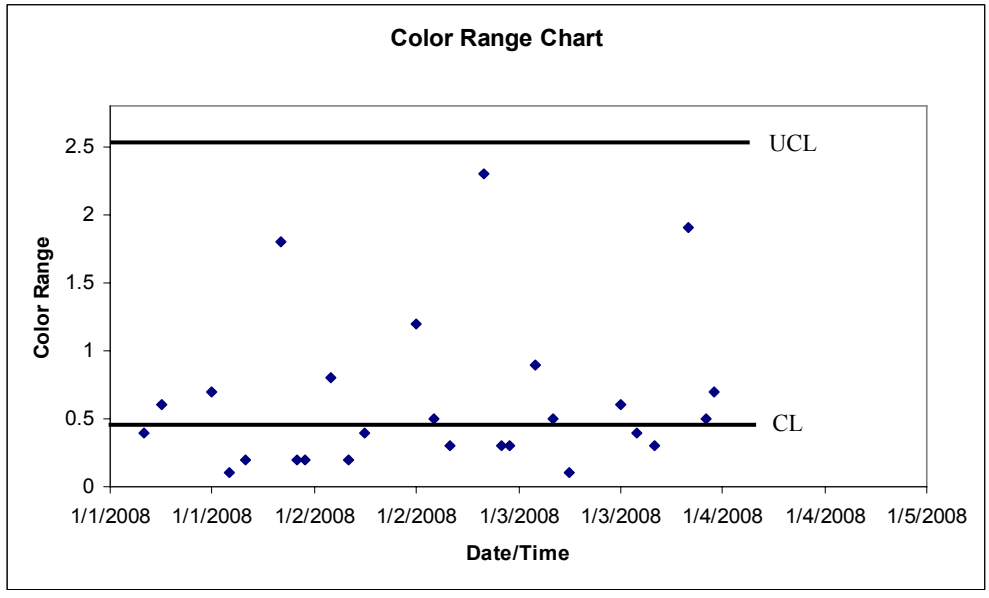
Observation	Alcohol (%v/v)
1	4.1
2	4.15
3	4.09
4	4.08
5	4.13
6	4.3
7	4.06
8	4.12
9	4.08

10	4.05
11	3.95
12	4.15
13	4.16
14	4.15
15	4.18
16	4.15
17	4.17
18	4.2
19	4.09
20	4.07
21	4.15
22	4.09
23	4.12
24	4.13
25	4.21
26	4.19
27	4.17
28	4.15
29	4.13
30	4.1
31	4.08
32	4.05

Example 3

Control limits were established for a method to measure color. The method was determined to be in control and routine run and range charts are plotted below. The color measurement is conducted over 3 shifts with 3 control samples analyzed per shift.





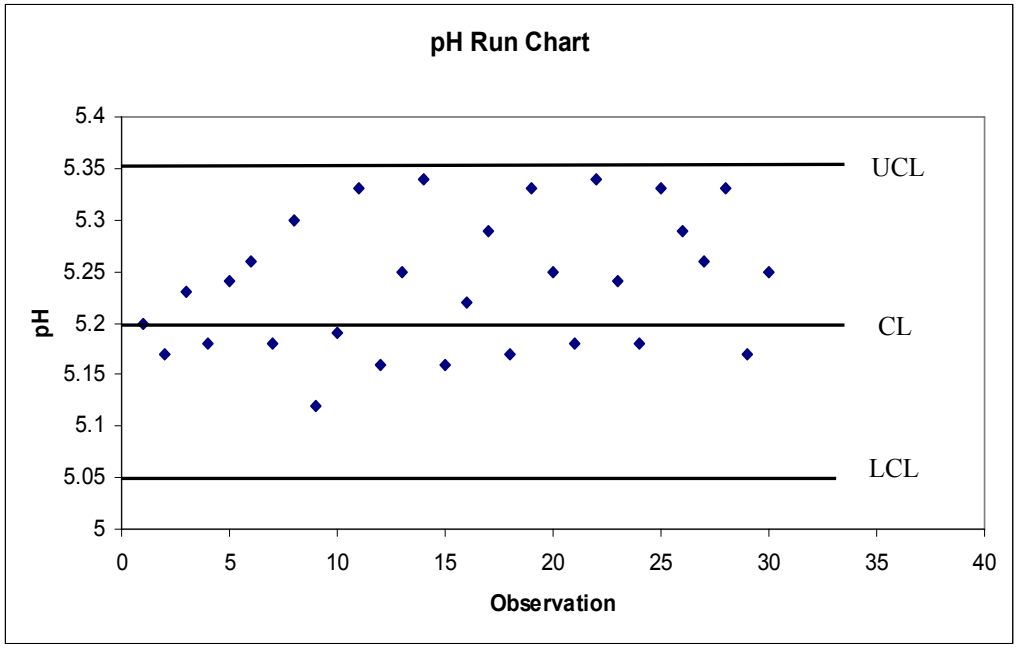
Analysis: None of the standard control chart rules have been violated in either of the plots. However, there is an unusual pattern in the data; the run chart appears to be clustered into 3 different regions per day (the first set on both sides of the center line, the second set above the center line, and the third set below the center line). The range chart also has one spike per day. Visual inspection shows that the data (cluster of three

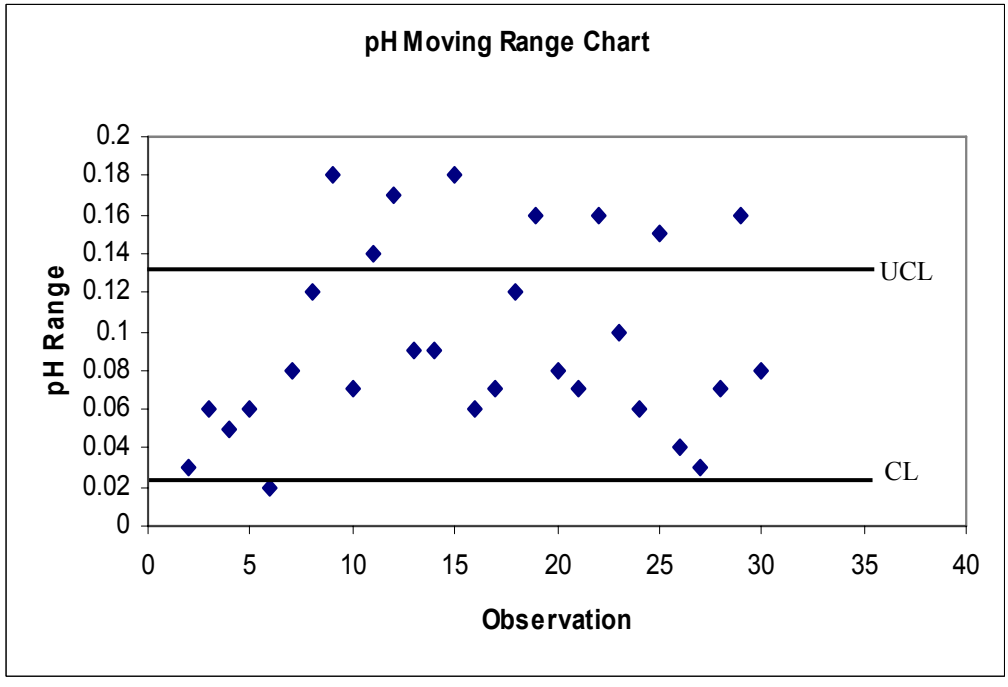
samples) is grouped by shift with the largest difference between the 2nd and 3rd sets (the spike in the range chart). Although none of the data are outside of the control rules, it is clear that there is a difference between how each shift runs the color method. A corrective action should be taken to eliminate the differences between shifts.

Observations	Color (SRM)	Difference
1/1/2008	12.1	
1/1/2008	12.5	0.4
1/1/2008	11.9	0.6
1/1/2008	12.6	0.7
1/1/2008	12.7	0.1
1/1/2008	12.9	0.2
1/1/2008	11.1	1.8
1/1/2008	11.3	0.2
1/1/2008	11.5	0.2
1/2/2008	12.3	0.8
1/2/2008	12.5	0.2
1/2/2008	12.1	0.4
1/2/2008	13.3	1.2
1/2/2008	12.8	0.5
1/2/2008	13.1	0.3
1/2/2008	10.8	2.3
1/2/2008	11.1	0.3
1/2/2008	11.4	0.3
1/3/2008	12.3	0.9
1/3/2008	11.8	0.5
1/3/2008	11.9	0.1
1/3/2008	12.5	0.6
1/3/2008	12.9	0.4
1/3/2008	13.2	0.3
1/3/2008	11.3	1.9
1/3/2008	10.8	0.5
1/3/2008	11.5	0.7

Example 4

Control limits were established for a method to measure wort pH. The method was determined to be in control and routine run and range charts are plotted below.





Analysis: The run chart shows that all of the data is within the control limits. The moving range charts shows a number of points above the UCL, suggesting that the repeatability of the measurement system has deteriorated.

Observation	pH	Difference
1	5.2	
2	5.17	0.03
3	5.23	0.06
4	5.18	0.05
5	5.24	0.06
6	5.26	0.02
7	5.18	0.08
8	5.3	0.12
9	5.12	0.18
10	5.19	0.07
11	5.33	0.14
12	5.16	0.17
13	5.25	0.09
14	5.34	0.09
15	5.16	0.18
16	5.22	0.06
17	5.29	0.07
18	5.17	0.12
19	5.33	0.16
20	5.25	0.08
21	5.18	0.07
22	5.34	0.16
23	5.24	0.1
24	5.18	0.06
25	5.33	0.15
26	5.29	0.04
27	5.26	0.03
28	5.33	0.07
29	5.17	0.16
30	5.25	0.08

Click here to go to the Control Charting Worksheets