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ABSTRACT

Statistical process controls are often used for monitoring processes to identify special causes of variation. Signals generated can assess the operational status of equipment and indicate when corrective action is needed. Control charts are a major tool in statistical process controls used in pharmaceutical manufacturing. It uses graphs as a statistical means of expressing the quality of a process or product. Quality improvement is inversely proportional to variability so that decreasing variabilities in product or process increases quality. Medicines testing laboratories employ various equipment to conduct analysis and generate reports to confirm a sample's disposition. To ensure data integrity, laboratory equipment is routinely calibrated. In many low-income countries, this causes a great financial burden. This study, therefore, investigated the use of control charts to monitor the performance of laboratory equipment in between calibrations schedules. Also, to explore the use of the *R, x.,* and *s* charts as an improvement over the use of 2SD and 3SD charts employed in earlier work.

Short-term variations from process estimates were generated for 3 pieces of lab equipment. For all processes, quality control samples with established quality matrices were selected as reference materials for monitoring each equipment's performance. The results from the control samples were inputted into the formulae for *R, x,* and *s* charts.

The estimates generated from the control samples were used to generate variable charts for process monitoring of various equipment. The charts graphically displayed the quality characteristics measured from the control samples over time. Control limits were chosen to contain approximately 99.73% of all data points. Out-of-control status of the equipment was also readily identified by data points outside the control limits.

Control limits generated from the charts' data indicated levels of equipment control and the control charts provide evidence of equipment monitoring.

Keywords: statistical process controls, quality control samples, control charts, control limits, and accreditation

Introduction

Monitoring a process makes it easier to detect variations that can lead to poor product quality. The performance of pieces of equipment used in Quality Control (QC) laboratories can be monitored through the use of statistical process charts (SPC). These charts are generated from data derived from

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processes and products and can serve as indicators for when an equipment's state of control is maintained or lost. There are quality characteristics that should be maintained by a process or product and are used to generate SPCs so that any variation observed is attributable to other variables such as the equipm ent.

Previous studies have elaborated on the use of R, *s*, and *x* in automobile and other service industries. Control charts derived from 2 and 3 standard deviations have also been reported in the literature. However, there seems to be a paucity of work on the use of SPC in laboratories within the regulatory sectors, especially in low-income economies. The cost of regular calibration of equipment is prohibitive for many laboratories in these regions, but that should not form a barrier to the quality of data they generate. To augment equipment calibration services, SPC monitoring can be employed to ensure data integrity. This research seeks to provide a scientific rationale for the use of statistical control charts to monitor the performance of laboratory equipment using a cost-effective model.

This project was a collaborative effort organized under Purdue University's Biotechnology Innovation and Regulatory Sciences (BIRS) program. It involved participants from the QC laboratories of the National Medicines Regulatory Authorities (NMRA) in Nigeria and Uganda, as well as some other Pharma industries in sub-Saharan Africa

Background

Control Charts as a tool in Statistical Process Controls and Product Quality

To manufacture goods that satisfy customers, a process must be stabilized with minimum variability to factors that change the target or nominal attributes required for optimal product quality. Therefore, manufacturers use Statistical Process Control (SPC) as a set of problem-solving tools to reduce variability, achieve process stability, and ultimately maintain product quality. Control charts are one of the seven major tools in SPC used in many areas of manufacturing (Montgomery, 2013)

The use of control charts as a means of monitoring the quality of a product was introduced by W.A Shewhart, who worked at AT & T Bell Laboratory in 1924. He described the use of graphs as a statistical means of expressing the quality of a product (Elkinton, 1932). Today, control charts are useful for in-process monitoring, being one of the primary techniques of statistical process control (SPC), it serves as a feedback mechanism to detect when corrective actions are required (Montgomery, 2013).

SPC has been linked to product quality and customer satisfaction. Quality has been defined through several philosophical lenses; each school of thought described the concept of quality through different, yet similar overall perspectives (Kulis & Mrduljas, 2009). There has been difficulty in using a universal definition for quality due to differences in perspectives as various interests influence the choice of the definition (Evans, 2014; Garvin, 1987). A modern definition describes quality as being inversely proportional to variability so that decreasing variabilities in product characteristics increases quality. Though some levels of natural variations are inherent in every system, assignable causes are undesirable and are responsible for poor quality products "Quality improvement is the reduction of variability in processes and products" (Montgomery, 2013). In laboratory procedures, variability in output data from QC samples can be used to assess equipment performance (Mercy Amaka Okezue, Clase, & Byrn, 2018).

Medicines testing laboratories use quality control activities to ensure they generate reliable test results. To conduct these tests, these laboratories use various equipment to conduct analysis and generate data to confirm a sample's disposition against recommended specifications. In the pharmaceutical industry, control charts are widely used to monitor process variability (Eissa, 2018; Riaz & Muhammad, 2012; Tôrres, Grangeiro Jr, & Fragoso, 2017). Therefore, for QC laboratories, we propose that properly calibrated equipment operates under some levels of predictable natural variations. These natural variations can be used to set control limits for charts that will monitor the performance of laboratory equipment. With control charts, abnormal or assignable sources of variations, deleterious to a testing process will be readily discovered and resolved.

Challenges with Calibrating Lab Equipment for Low-Income Countries

Quality control laboratories use several pieces of equipment to conduct analysis and generate data for test reports. To ensure reliable data are consistently produced, it is recommended laboratory equipment is routinely calibrated against traceable primary standards (Bucher, 2007). In many low-income countries, due to a lack of technical skills, these pieces of equipment are calibrated by experts from overseas countries. This causes a great financial burden on the costs to maintain laboratories in these regions. Aside from these scheduled annual or bi-annual verification activities, there is a need to assure these equipment is working optimally in between periods of calibrations. This study, therefore, seeks to investigate the use of control charts to monitor the performance of laboratory

equipment at shorter time intervals in between calibrations.

The theoretical basis for the study

Medicine testing laboratories use control samples to continually check the accuracy and precision of a procedure. The World Health Organization (WHO) recommends that such samples should have a matrix similar to materials routinely analyzed using laboratory equipment. A further recommendation is that these reference samples should have assigned value and be handled in the same manner as other reference standards used in laboratory testing (World Health Organization, 2010). This study theorizes that laboratory equipment and process performances can be monitored with charts that use control limits to display variations in output data from routine analysis of assigned reference samples. When sample output data plots in a random manner within the set limits, the system is said to be in a state of control. Conversely, the process is out of control, when points plot outside these limits or exhibit a non-random trend (Montgomery, 2013). Ultimately, a control chart can be used to monitor equipment or process performance variability over periods of use, and thereby detect assignable or cause variations. When such process variability occurs, it often triggers investigations to determine factors that led to the out-of-control status. Early and accurate detection of the presence of these undesirable assignable sources of variation will reduce laboratory process and equipment errors.

Use of control charts in medicine testing laboratories

A typical control chart investigates long or short-term process variations. Levey-Jennings (LJ) charts investigate long-term variations on factors that impact product quality, while grand mean (*X),* average range *(R),* and standard deviation (*s)* charts, are used in short term. LJ charts are run charts that set control limits within 3 standard deviations (SD) units from the mean (μ) value, such that the lower control limit is μ + 3SD, while the lower control limit is set at μ - 3SD (Drain, 1997; Schmidt, Walker, & Pearson, 2018; V. Roberts & S. Tsay, 1996). In many manufacturing and service industries, different types of variable and attribute control charts are used for process monitoring. The use of a combination of *x* and *s*, or *x* and *R* control charts, has the advantage that both process centering and variability is monitored independently. This has been shown to achieve better decisions when investigating assignable causes for out-of-control results (Montgomery, 2013).

Recommendations for Estimating Control Limits for SPC

Several authors recommended using short-term variations from process estimates to set the limits used for control charts. These estimates can be used to generate variable *R, x*, and *s* charts used for process monitoring (Leavenworth & Grant, 2000; Montgomery, 2013; Qiu, 2013; Vardeman & Jobe, 2016; Wadsworth, Stephens, & Godfrey, 2002; Wheeler, 1995). An alternative approach is the use of long-term variations, such as Levy-Jenning charts, to set control limits that detect process variations (Gras, 2017; Mercy Amaka Okezue et al., 2018; Westgard et al., 2006; Westgard & Westgard, 2017)

Some General Rules for Examining a Control Chart to Determine Whether the Process is in Control

1. No data plots outside the control limits
2. There should be approximately equal numbers of data plots above and below the centerline
3. The process will have points that seem to fall randomly above and below the centerline.
4. Most points, but not all, are near the centerline, and only a few are close to the control limits
5. When a process is in statistical control, the pattern of points fluctuates randomly between the control limits with no recognizable pattern (Evans, 2014; Montgomery, 2013).

Methods

1. Volunteers analysts were chosen from the QC laboratories of the NMRAs in Nigeria and Uganda
2. All participants were trained on the project objectives and criteria for selecting samples and equipment

2.1 Criteria for selecting Quality Control (QC) samples

2.1.1 The matrix should be similar to that of the products normally analyzed using the equipment

2.1.2 The sample size should be adequate for generating the initial 25 - 30 data points needed to determine the control limits for the SPC charts

2.1.3 The sample should be stable when maintained under the specified storage conditions

2.1.4 The equipment operators must be qualified to accurately assess the

samples using a specified method of analysis

2.1.5 If the sample is changed, a new set of data may be required to generate another chart for monitoring. Especially when out of trends SPC results are obtained as a result of the change.

The QC samples which met the above-stated criteria were chosen for monitoring various pieces of laboratory equipment, namely: UV-spectrophotometers, analytical weighing balance, and high-performance liquid chromatography (HPLC). The QC samples were maintained as reference materials under the specified storage conditions as presented in the product labels.

2.2 Criteria for selecting personnel, equipment, and reagents for the study

2.2.1 Each analyst must have received adequate training for the tests they conduct in their respective NMRAs

2.2.2 Each piece of equipment must be under calibration and adequate maintenance

2.2.3 All reagents used must be of the appropriate grade for the study

3. All the project participants received a BIRS structured training on how to generate data, and plot R, *s*, and *x* charts for statistical process monitoring of the various laboratory equipment.

3.1 Monitoring HPLC through data from analysis of ciprofloxacin certified material

3.1.1 Ciprofloxacin hydrochloride secondary standard lot number: LRAB3671, from Merck Sigma-Aldrich Germany, was assayed using a USP Ciprofloxacin HCl USP CRS Lot No.: J1L040. The USP/NF method for the material was adapted as the method for analysis. An HPLC Agilent1260 Infinity II system fitted with a UV (DAD) detector set at 278nm was used. A Luna Phenomenex C18 column with 250 X 4.6 mm, particle size 5uM dimensions was employed for separating the sample components using a run time of 12 minutes, 5uL injection volume set at 1.5ml/minute, and the column temperature was maintained at 40^{o}C. Mobile phase: 13 volumes of acetonitrile and 87 volumes of solution A. Prepared solution A from 0.245%w/v solution of orthophosphoric acid in Type 1 water and adjusted the pH of the resultant solution to 3.0 using Triethylamine.

3.2 Monitoring UV-spectrophotometer through data from analysis of acetaminophen tablets.

3.2.1 Acetaminophen 500mg packed as 1x 1000 tablets, lot:34757, was assayed using the British Pharmacopeia (BP) method. A Perkin Elmer Lambda 35 UV-Spectrophotometer set at 257nm was used to determine the content of acetaminophen in the tablets.

3.3 Monitoring an analytical weighing balance through data from verification of a certified 200mg standard weight.

3.3.1 The Mettler Toledo analytical balance used had the following details- model: XSE205DU, serial no: B431872408, Ø Calibration Certificate No: 20201006006 (As calibrated by NQA&CA). The QC sample used was a certified 20mg standard weight, manufactured by MSME, model 123.04, serial #: 50216, Ø Calibration Certificate No: 20210130001 (As calibrated by NQA&CA). Measurement Uncertainty (As Stated on The Certificate) was ± 0.008mg.

4.0 The first phase of the control charts was initiated by gathering retrospective data from 30 data points to analyzing the QC samples specified for each piece of equipment.

4.1 The following equations and assumptions were used for determining the control limits for the R and $\bar{X}$ charts:

Suppose that a quality characteristic (assay value or weight determination) is normally distributed with a mean value μ, and a standard deviation *s*. If x_1, $x_2 \ldots x_n$ is a sample of size n, then the average of this sample is determined using Equation 1

$$\bar{X} = \frac{\mathrm{X1} + \mathrm{X2} \ldots \mathrm{Xn}}{n} \qquad \text{Equation 1}$$

The average of each sample was represented by $\bar{X}1, \bar{X}2 \ldots . \bar{X}n$. If m samples were available, each containing n observations of the quality characteristics, then the process average μ, was estimated using the grand average calculated with Equation 2

$$\bar{\bar{X}} = (\bar{X}_{1+} \bar{X}_{2 \ldots\ldots +} \bar{X}_{m}) / \mathrm{m} \qquad \text{Equation 2}$$

Range R, and average range $\bar{R}$, which were used as an estimate for δ, were determined using Equations 3 and 4.

$$R = x_{max} - x_{min} \qquad \text{Equation 3}$$

$\bar{R}$= (R_1 + R_2…+R_m) /m Equation 4

The control limits for the $\bar{X}$ and *R* charts were determined as follows:

Control limits for the $\bar{X}$ charts	Control limits for the R charts
Upper control limit (UCL) = $\bar{\bar{X}}$ + $A_2\bar{R}$	UCL = $D_4\bar{R}$
Center Line (CL) = $\bar{\bar{X}}$	CL = $\bar{R}$
Lower Control Limit (LCL) = $\bar{\bar{X}}$ - $A_2\bar{R}$	LCL = $D_3\bar{R}$

The constants A2, D2, and D3 were obtained from the statistics table titled: Factors for Constructing Variables Control Charts, see Table 1 in the Appendix section of this manuscript

4.2 The following equations and assumptions were used for determining the control limits for the *s* and $\bar{X}$ charts:

Standard deviation *s* is the square root of the variance, and the sample variance s^2 was determined using Equation 5

$$s^2 = \frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1} \qquad s = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1}}$$ Equation 5

The control limits for the $\bar{X}$ and *s* charts were determined as follows:

Control limits for the $\bar{X}$ charts	Control limits for the s charts
UCL = $\bar{\bar{X}}$ + $A_3\bar{s}$	UCL = $B_4\bar{s}$
CL = $\bar{\bar{X}}$	CL = $\bar{s}$
LCL = $\bar{\bar{X}}$ – $A_3\bar{s}$	LCL = $B_3\bar{s}$

5. The participants independently uploaded their data to a secured OneDrive platform provided by the BIRS center.
6. The project team met regularly to review the data and provide required feedback to participants.

Results

For this project, the data obtained for phase 1 were used to construct trial control limits. These limits were used to determine if the processes had been in control over the period during which the data were collected, and to see if they can be used to monitor the future performance of the lab equipment. The analysts from the NMRAs generated data that were used to set the control limits for monitoring the 3 pieces of laboratory equipment investigated as exemplars in this project.

1. SPC for monitoring the performance of the HPLC

The data generated from the ciprofloxacin QC sample was used to construct the trial control limits for the *R*, *s*, and $\bar{X}$ charts shown in Figure 1.

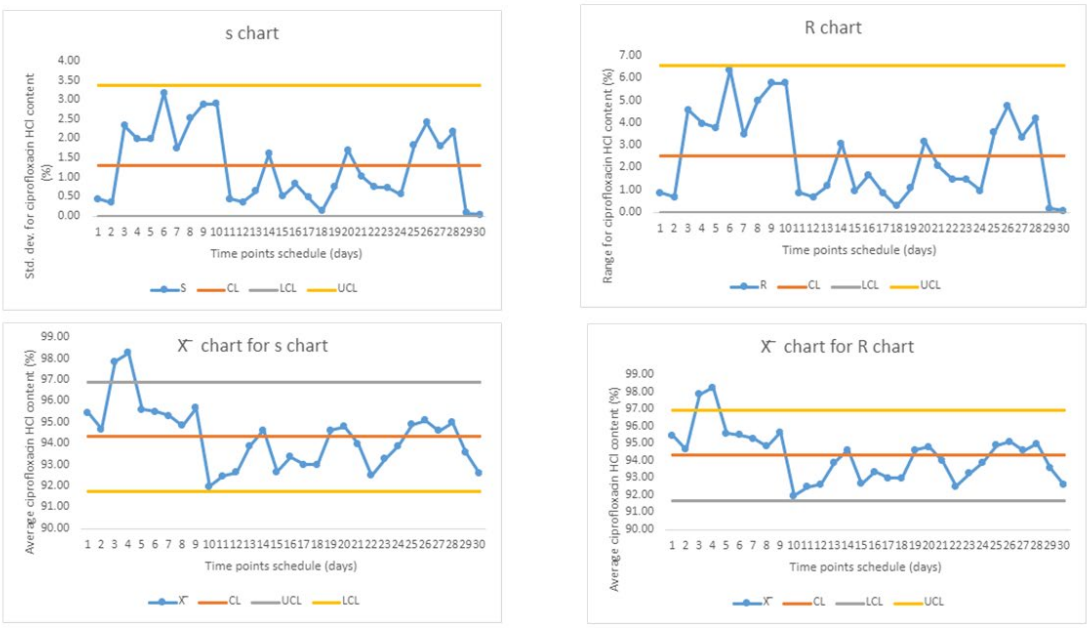

Figure 1 *R*, *s* and $\bar{X}$ charts generated from ciprofloxacin QC analysis were used to set control limits for monitoring HPLC lab equipment for phase 1

Two out of the thirty data points generated were outside the upper control limits for the *s* and *R* charts. Following the protocol for the study, a root cause investigation was carried out to determine if they were assignable to the QC sample or the HPLC systems. The sample size for setting the control limits was adjusted to exclude the two data sets after the investigation provided plausible reasons for the out-of-trend data. The reasons were traceable to human error, so new control limits were recalculated using 28 data points as shown in Figure 2

Figure 2 *R*, *s,* and $\bar{X}$ charts generated after excluding the 2 data points from ciprofloxacin QC analysis. New control limits were set for monitoring HPLC lab equipment for phase 1

All the experimental data generated for the ciprofloxacin QC sample is provided in the Appendix section as Tables 2 and 3.

The data generated from the assays of the acetaminophen tablets QC sample was used to construct the trial control limits for the *R*, *s*, and $\bar{X}$ charts shown in Figure 3.

1. SPC for monitoring performance of the UV-Spectrophotometer

Figure 3 *R*, *s* and $\bar{X}$ charts generated from analysis of the acetaminophen tablets QC sample was used to set control limits for monitoring a piece of UV-Spectrophotometer lab equipment for phase 1

All the experimental data generated for the acetaminophen QC sample is provided in the Appendix section as Tables 4 and 5.

The data generated from the certified 20mg standard weight QC sample was used to construct the trial control limits for the *R*, *s*, and $\bar{X}$ charts shown in Figure 4.

1. SPC for monitoring performance of the Analytical Balance

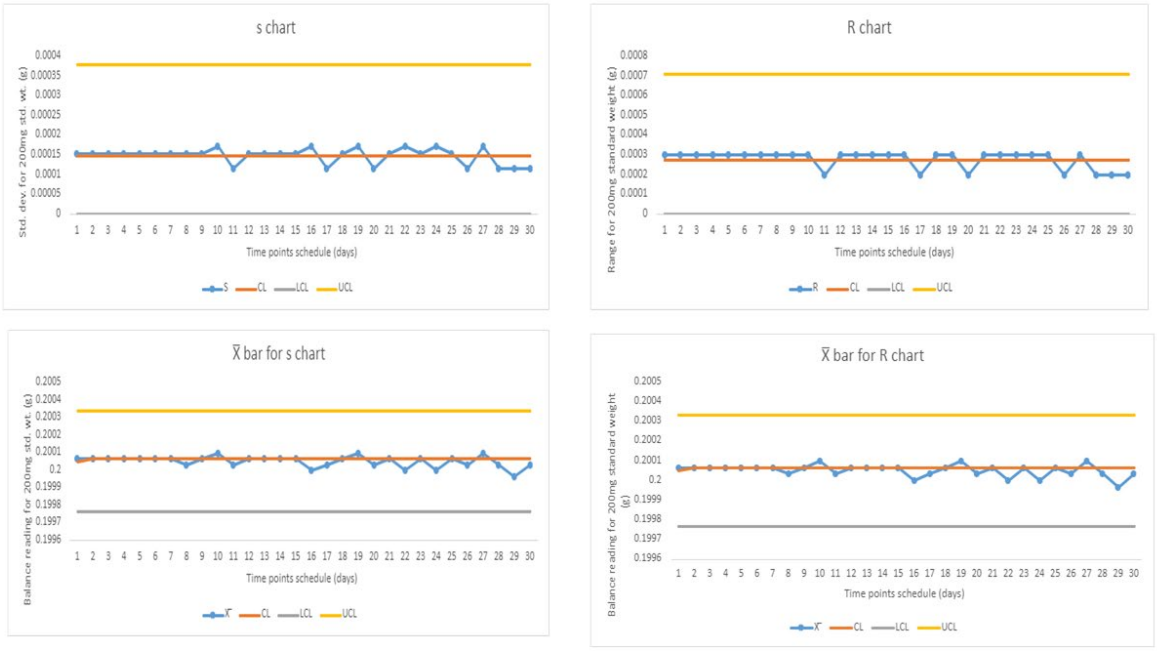

Figure 4 *R*, *s,* and $\bar{X}$ charts generated from the certified 20mg standard weight QC sample was used to set control limits for monitoring an analytical balance lab equipment for phase 1

All the experimental data generated from the weight verification of the certified 20mg standard weight QC sample is provided in the Appendix section as Table 6.

Discussions

The results obtained from this study provide further evidence on the advantages of the use of short-term range run charts, which measures both processes centering and variability independently. The resulting SPC charts can be used to monitor laboratory equipment or process performance. This is similar to other studies which investigated the use of short-range run charts over the long-term process variations using Levey-Jennings (LJ) charts (Sharma, 2011; Vani et al., 2016). Schmidt and his colleagues also compared the 2 systems for setting the limits for control charts in a laboratory setting. They discovered that the use of short-term estimates provided control limits that enabled easier detection of process shifts. And, suggested laboratories will achieve higher accuracies using *R*-charts than LJ charts (Schmidt et al., 2018). We submit that the LJ charts formerly used in our quality control labs (Mercy Amaka Okezue et al., 2018), have a draw-back of using a single chart for monitoring the stability of equipment and processes. And similar to our current concerns, Schmidt and his colleagues suggested that the limits set by these types of charts may be too wide so that out-of-control statuses are not readily detected (Schmidt et al., 2018). This collaborative study, therefore, introduces the use of *x* and *s*, or *x* and *R,* and other attribute control charts in monitoring the stability of laboratory equipment and procedures.

SPCs are also important for determining measurements (MU) of uncertainties for QC laboratories. Especially if they want to attain international accreditation against ISO17025 and WHO Good Practices for Pharmaceutical QC laboratories. These laboratory standards have requirements that a testing facility should determine the MU associated with tests they conduct, which may be used to verify the accuracy of their test results. MU determinations are especially required for certain categories of test reports such as; enforcement samples that may lead to litigations, and samples with borderline results. They may also be instances where MU is based on a lab customer's requests (International Standard Organisation, 2017; World Health Organization, 2010). The inability of laboratories in low-income economies to demonstrate MU has been reported as one of the causes of not attaining international accreditation (Mercy A. Okezue, Adeyeye, Byrn, Abiola, & Clase, 2020; Plebani, Padoan, & Sciacovelli, 2020; Taverniers, De Loose, & Van Bockstaele, 2004).

Use of control charts in determining Process capabilities

In addition to monitoring stability, control charts also provide valuable information about process capabilities, Cp and Cpk. Process capability is the

ability to deliver outputs that meet product specifications, so the knowledge of Cp and Cpk is important for technical and business decisions in quality control laboratories and other fields. (Montgomery, 2013). Apart from the use of Cp and Cpk as the index for measurement of process capability, some authors have used other parameters such as SR ratio near one as stability-indicating. I_{NSR} measures the ratio between the number of subgroups that fail the western electric rules, to the total number of subgroups assessed. A ratio greater than 1.089% indicated instability for a sample size of 1,000 or more. Whereas, a 4.5% cut-off value was assigned for sample sizes less than 1,000 units (B. Ramirez & G. Runger, 2006; Wheeler, 1995).

Moving into the Second Phase of establishing SPC

Control limits were calculated based on the data generated from the QC samples. At the initial phase of establishing SPC, the objective of the analyst is to understand the natural variations that are inherent in a system, and so some data points may fall outside the expected trends. Such incidents are investigated and the potential assignable causes are mitigated. Thereafter, the data are excluded, and a new set of control limits is recalculated (Montgomery, 2013).

The next step, phase 2, is initiated after a “clean” set of process data are achieved; these should be collected under stable conditions and representative

of the in-control process performance of the lab equipment. In this latter phase, the control charts are used to monitor the lab equipment by comparing the sample statistic calculated for each successive sample to the control limits established in phase 1. The assumption is that the processes will become more stable in phase 2 because most of the potential assignable sources of variation would have been tackled in the prior phase. It is at this stage that the SPC charts can be effectively used to monitor the performance of the various pieces of laboratory equipment. Two alternative processes that can be used to monitor the process in phase 2 include the exponentially weighted moving average (EWMA) control chart, as well as the cumulative sum (CUSUM) control chart (Montgomery, 2013). These form the future focus for this project, as more data points are generated to generate the required statistic for constructing the EWMA and CUSUM charts.

Conclusion

Laboratory equipment is said to be in a state of control when operating within its natural tolerance limits. When stored under their recommended conditions, QC samples can be used to generate data to plot SPC charts for monitoring the performance of some pieces of lab equipment. Statistics from these samples were used to generate control limits for monitoring the performance of an HPLC, UV-spectrophotometers, and analytical weighing balance. SPC monitoring of these pieces of equipment complements other calibration efforts to ensure the reliability of lab data and can facilitate laboratory accreditation.

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Appendix Section

Table 1 The values for constants A2, D2, and D3 used in calculating the control limits for *R, s*, and *X* charts

Factors for Constructing Variables Control Charts

Observations in Sample, n	Chart for Averages: Factors for Control Limits			Chart for Averages: Factors for Center Line		Chart for Standard Deviations: Factors for Control Limits				Chart for Standard Deviations: Factors for Center Line		Chart for Ranges: Factors for Control Limits				
	A	A_2	A_3	c_4	$1/c_4$	B_3	B_4	B_5	B_6	d_2	$1/d_2$	d_3	D_1	D_2	D_3	D_4
2	2.121	1.880	2.659	0.7979	1.2533	0	3.267	0	2.606	1.128	0.8865	0.853	0	3.686	0	3.267
3	1.732	1.023	1.954	0.8862	1.1284	0	2.568	0	2.276	1.693	0.5907	0.888	0	4.358	0	2.574
4	1.500	0.729	1.628	0.9213	1.0854	0	2.266	0	2.088	2.059	0.4857	0.880	0	4.698	0	2.282
5	1.342	0.577	1.427	0.9400	1.0638	0	2.089	0	1.964	2.326	0.4299	0.864	0	4.918	0	2.114
6	1.225	0.483	1.287	0.9515	1.0510	0.030	1.970	0.029	1.874	2.534	0.3946	0.848	0	5.078	0	2.004
7	1.134	0.419	1.182	0.9594	1.0423	0.118	1.882	0.113	1.806	2.704	0.3698	0.833	0.204	5.204	0.076	1.924
8	1.061	0.373	1.099	0.9650	1.0363	0.185	1.815	0.179	1.751	2.847	0.3512	0.820	0.388	5.306	0.136	1.864
9	1.000	0.337	1.032	0.9693	1.0317	0.239	1.761	0.232	1.707	2.970	0.3367	0.808	0.547	5.393	0.184	1.816
10	0.949	0.308	0.975	0.9727	1.0281	0.284	1.716	0.276	1.669	3.078	0.3249	0.797	0.687	5.469	0.223	1.777
11	0.905	0.285	0.927	0.9754	1.0252	0.321	1.679	0.313	1.637	3.173	0.3152	0.787	0.811	5.535	0.256	1.744
12	0.866	0.266	0.886	0.9776	1.0229	0.354	1.646	0.346	1.610	3.258	0.3069	0.778	0.922	5.594	0.283	1.717
13	0.832	0.249	0.850	0.9794	1.0210	0.382	1.618	0.374	1.585	3.336	0.2998	0.770	1.025	5.647	0.307	1.693
14	0.802	0.235	0.817	0.9810	1.0194	0.406	1.594	0.399	1.563	3.407	0.2935	0.763	1.118	5.696	0.328	1.672
15	0.775	0.223	0.789	0.9823	1.0180	0.428	1.572	0.421	1.544	3.472	0.2880	0.756	1.203	5.741	0.347	1.653
16	0.750	0.212	0.763	0.9835	1.0168	0.448	1.552	0.440	1.526	3.532	0.2831	0.750	1.282	5.782	0.363	1.637
17	0.728	0.203	0.739	0.9845	1.0157	0.466	1.534	0.458	1.511	3.588	0.2787	0.744	1.356	5.820	0.378	1.622
18	0.707	0.194	0.718	0.9854	1.0148	0.482	1.518	0.475	1.496	3.640	0.2747	0.739	1.424	5.856	0.391	1.608
19	0.688	0.187	0.698	0.9862	1.0140	0.497	1.503	0.490	1.483	3.689	0.2711	0.734	1.487	5.891	0.403	1.597
20	0.671	0.180	0.680	0.9869	1.0133	0.510	1.490	0.504	1.470	3.735	0.2677	0.729	1.549	5.921	0.415	1.585
21	0.655	0.173	0.663	0.9876	1.0126	0.523	1.477	0.516	1.459	3.778	0.2647	0.724	1.605	5.951	0.425	1.575
22	0.640	0.167	0.647	0.9882	1.0119	0.534	1.466	0.528	1.448	3.819	0.2618	0.720	1.659	5.979	0.434	1.566
23	0.626	0.162	0.633	0.9887	1.0114	0.545	1.455	0.539	1.438	3.858	0.2592	0.716	1.710	6.006	0.443	1.557
24	0.612	0.157	0.619	0.9892	1.0109	0.555	1.445	0.549	1.429	3.895	0.2567	0.712	1.759	6.031	0.451	1.548
25	0.600	0.153	0.606	0.9896	1.0105	0.565	1.435	0.559	1.420	3.931	0.2544	0.708	1.806	6.056	0.459	1.541

Table 2 Data from HPLC analysis of ciprofloxacin QC sample used to generate the control limits for the SPC

PERCENTAGE ASSAY FOR CIPLOFLOXACIN BY HPLC

Days	ASSAY REPLICATES			X -bar for R-chart				R				S				X-bar for s-chart			
	Assay 1	Assay 2	Assay 3	$\bar{X}$	CL	LCL	UCL	R	CL	LCL	UCL	S	CL	LCL	UCL	$\bar{X}$	CL	UCL	LCL
1	95.00	95.60	95.90	95.50	94.36	91.73	96.98	0.90	2.57	0.00	6.61	0.46	1.33	0.00	3.40	95.50	94.36	96.94	91.77
2	94.60	95.10	94.40	94.70	94.36	91.73	96.98	0.70	2.57	0.00	6.61	0.36	1.33	0.00	3.40	94.70	94.36	96.94	91.77
3	95.30	99.90	98.50	97.90	94.36	91.73	96.98	4.60	2.57	0.00	6.61	2.36	1.33	0.00	3.40	97.90	94.36	96.94	91.77
4	96.20	100.20	98.50	98.30	94.36	91.73	96.98	4.00	2.57	0.00	6.61	2.01	1.33	0.00	3.40	98.30	94.36	96.94	91.77
5	94.90	94.10	97.90	95.63	94.36	91.73	96.98	3.80	2.57	0.00	6.61	2.00	1.33	0.00	3.40	95.63	94.36	96.94	91.77
6	98.70	92.30	95.60	95.53	94.36	91.73	96.98	6.40	2.57	0.00	6.61	3.20	1.33	0.00	3.40	95.53	94.36	96.94	91.77
7	95.50	93.50	97.00	95.33	94.36	91.73	96.98	3.50	2.57	0.00	6.61	1.76	1.33	0.00	3.40	95.33	94.36	96.94	91.77
8	95.40	92.10	97.10	94.87	94.36	91.73	96.98	5.00	2.57	0.00	6.61	2.54	1.33	0.00	3.40	94.87	94.36	96.94	91.77
9	98.50	92.70	95.90	95.70	94.36	91.73	96.98	5.80	2.57	0.00	6.61	2.91	1.33	0.00	3.40	95.70	94.36	96.94	91.77
10	94.70	92.40	88.90	92.00	94.36	91.73	96.98	5.80	2.57	0.00	6.61	2.92	1.33	0.00	3.40	92.00	94.36	96.94	91.77
11	92.10	93.00	92.40	92.50	94.36	91.73	96.98	0.90	2.57	0.00	6.61	0.46	1.33	0.00	3.40	92.50	94.36	96.94	91.77
12	92.50	93.10	92.40	92.67	94.36	91.73	96.98	0.70	2.57	0.00	6.61	0.38	1.33	0.00	3.40	92.67	94.36	96.94	91.77
13	94.70	93.60	93.50	93.93	94.36	91.73	96.98	1.20	2.57	0.00	6.61	0.67	1.33	0.00	3.40	93.93	94.36	96.94	91.77
14	94.10	93.40	96.50	94.67	94.36	91.73	96.98	3.10	2.57	0.00	6.61	1.63	1.33	0.00	3.40	94.67	94.36	96.94	91.77
15	92.50	92.30	93.30	92.70	94.36	91.73	96.98	1.00	2.57	0.00	6.61	0.53	1.33	0.00	3.40	92.70	94.36	96.94	91.77
16	92.60	93.30	94.30	93.40	94.36	91.73	96.98	1.70	2.57	0.00	6.61	0.85	1.33	0.00	3.40	93.40	94.36	96.94	91.77
17	93.60	92.70	92.80	93.03	94.36	91.73	96.98	0.90	2.57	0.00	6.61	0.49	1.33	0.00	3.40	93.03	94.36	96.94	91.77
18	92.90	93.00	93.20	93.03	94.36	91.73	96.98	0.30	2.57	0.00	6.61	0.15	1.33	0.00	3.40	93.03	94.36	96.94	91.77
19	95.20	94.10	xx	94.65	94.36	91.73	96.98	1.10	2.57	0.00	6.60	0.78	1.33	0.00	3.40	94.65	94.36	96.94	91.77
20	94.10	96.80	93.60	94.83	94.36	91.73	96.98	3.20	2.57	0.00	6.61	1.72	1.33	0.00	3.40	94.83	94.36	96.94	91.77
21	94.00	95.10	93.00	94.03	94.36	91.73	96.98	2.10	2.57	0.00	6.61	1.05	1.33	0.00	3.40	94.03	94.36	96.94	91.77
22	93.20	92.70	91.70	92.53	94.36	91.73	96.98	1.50	2.57	0.00	6.61	0.76	1.33	0.00	3.40	92.53	94.36	96.94	91.77
23	94.10	93.20	92.60	93.30	94.36	91.73	96.98	1.50	2.57	0.00	6.61	0.75	1.33	0.00	3.40	93.3	94.36	96.94	91.77
24	94.60	93.60	93.60	93.93	94.36	91.73	96.98	1.00	2.57	0.00	6.61	0.58	1.33	0.00	3.40	93.93	94.36	96.94	91.77
25	96.50	92.90	95.40	94.93	94.36	91.73	96.98	3.60	2.57	0.00	6.61	1.84	1.33	0.00	3.40	94.93	94.36	96.94	91.77
26	97.30	92.50	95.60	95.13	94.36	91.73	96.98	4.80	2.57	0.00	6.61	2.43	1.33	0.00	3.40	95.13	94.36	96.94	91.77
27	93.90	96.70	93.30	94.63	94.36	91.73	96.98	3.40	2.57	0.00	6.61	1.81	1.33	0.00	3.40	94.63	94.36	96.94	91.77
28	94.30	97.50	93.30	95.03	94.36	91.73	96.98	4.20	2.57	0.00	6.61	2.19	1.33	0.00	3.40	95.03	94.36	96.94	91.77
29	93.50	93.60	93.70	93.60	94.36	91.73	96.98	0.20	2.57	0.00	6.61	0.10	1.33	0.00	3.40	93.60	94.36	96.94	91.77
30	92.70	92.60	92.60	92.63	94.36	91.73	96.98	0.10	2.57	0.00	6.61	0.06	1.33	0.00	3.40	92.63	94.36	96.94	91.77
				94.4				**2.6**				**1.3**							

Table 3 Revised data from HPLC analysis of ciprofloxacin QC sample used to generate new control limits for the SPC

PERCENTAGE ASSAY FOR CIPLOFLOXACIN BY HPLC

Days	ASSAY REPLICATES			X -bar for R-chart				R				S				X-bar for s-chart			
	Assay 1	Assay 2	Assay 3	$\bar{X}$	CL	LCL	UCL	R	CL	LCL	UCL	S	CL	LCL	UCL	$\bar{X}$	CL	UCL	LCL
1	95.00	95.60	95.90	95.50	94.09	91.59	96.59	0.90	2.44	0.00	6.29	0.46	1.33	0.00	3.25	95.50	94.09	96.56	91.62
2	94.60	95.10	94.40	94.70	94.09	91.59	96.59	0.70	2.44	0.00	6.29	0.36	1.33	0.00	3.25	94.70	94.36	96.56	91.62
5	94.90	94.10	97.90	95.63	94.09	91.59	96.59	3.80	2.44	0.00	6.29	2.00	1.33	0.00	3.25	95.63	94.36	96.56	91.62
6	98.70	92.30	95.60	95.53	94.09	91.59	96.59	6.40	2.44	0.00	6.29	3.20	1.33	0.00	3.25	95.53	94.36	96.56	91.62
7	95.50	93.50	97.00	95.33	94.09	91.59	96.59	3.50	2.44	0.00	6.29	1.76	1.33	0.00	3.25	95.33	94.36	96.56	91.62
8	95.40	92.10	97.10	94.87	94.09	91.59	96.59	5.00	2.44	0.00	6.29	2.54	1.33	0.00	3.25	94.87	94.36	96.56	91.62
9	98.50	92.70	95.90	95.70	94.09	91.59	96.59	5.80	2.44	0.00	6.29	2.91	1.33	0.00	3.25	95.70	94.36	96.56	91.62
10	94.70	92.40	88.90	92.00	94.09	91.59	96.59	5.80	2.44	0.00	6.29	2.92	1.33	0.00	3.25	92.00	94.36	96.56	91.62
11	92.10	93.00	92.40	92.50	94.09	91.59	96.59	0.90	2.44	0.00	6.29	0.46	1.33	0.00	3.25	92.50	94.36	96.56	91.62
12	92.50	93.10	92.40	92.67	94.09	91.59	96.59	0.70	2.44	0.00	6.29	0.38	1.33	0.00	3.25	92.67	94.36	96.56	91.62
13	94.70	93.60	93.50	93.93	94.09	91.59	96.59	1.20	2.44	0.00	6.29	0.67	1.33	0.00	3.25	93.93	94.36	96.56	91.62
14	94.10	93.40	96.50	94.67	94.09	91.59	96.59	3.10	2.44	0.00	6.29	1.63	1.33	0.00	3.25	94.67	94.36	96.56	91.62
15	92.50	92.30	93.30	92.70	94.09	91.59	96.59	1.00	2.44	0.00	6.29	0.53	1.33	0.00	3.25	92.70	94.36	96.56	91.62
16	92.60	93.30	94.30	93.40	94.09	91.59	96.59	1.70	2.44	0.00	6.29	0.85	1.33	0.00	3.25	93.40	94.36	96.56	91.62
17	93.60	92.70	92.80	93.03	94.09	91.59	96.59	0.90	2.44	0.00	6.29	0.49	1.33	0.00	3.25	93.03	94.36	96.56	91.62
18	92.90	93.00	93.20	93.03	94.09	91.59	96.59	0.30	2.44	0.00	6.29	0.15	1.33	0.00	3.25	93.03	94.36	96.56	91.62
19	95.20	94.10	xx	94.65	94.09	91.59	96.59	1.10	2.44	0.00	6.29	0.78	1.33	0.00	3.25	94.65	94.36	96.56	91.62
20	94.10	96.80	93.60	94.83	94.09	91.59	96.59	3.20	2.44	0.00	6.29	1.72	1.33	0.00	3.25	94.83	94.36	96.56	91.62
21	94.00	95.10	93.00	94.03	94.09	91.59	96.59	2.10	2.44	0.00	6.29	1.05	1.33	0.00	3.25	94.03	94.36	96.56	91.62
22	93.20	92.70	91.70	92.53	94.09	91.59	96.59	1.50	2.44	0.00	6.29	0.76	1.33	0.00	3.25	92.53	94.36	96.56	91.62
23	94.10	93.20	92.60	93.30	94.09	91.59	96.59	1.50	2.44	0.00	6.29	0.75	1.33	0.00	3.25	93.3	94.36	96.56	91.62
24	94.60	93.60	93.60	93.93	94.09	91.59	96.59	1.00	2.44	0.00	6.29	0.58	1.33	0.00	3.25	93.93	94.36	96.56	91.62
25	96.50	92.90	95.40	94.93	94.09	91.59	96.59	3.60	2.44	0.00	6.29	1.84	1.33	0.00	3.25	94.93	94.36	96.56	91.62
26	97.30	92.50	95.60	95.13	94.09	91.59	96.59	4.80	2.44	0.00	6.29	2.43	1.33	0.00	3.25	95.13	94.36	96.56	91.62
27	93.90	96.70	93.30	94.63	94.09	91.59	96.59	3.40	2.44	0.00	6.29	1.81	1.33	0.00	3.25	94.63	94.36	96.56	91.62
28	94.30	97.50	93.30	95.03	94.09	91.59	96.59	4.20	2.44	0.00	6.29	2.19	1.33	0.00	3.25	95.03	94.36	96.56	91.62
29	93.50	93.60	93.70	93.60	94.09	91.59	96.59	0.20	2.44	0.00	6.29	0.10	1.33	0.00	3.25	93.60	94.36	96.56	91.62
30	92.70	92.60	92.60	92.63	94.09	91.59	96.59	0.10	2.44	0.00	6.29	0.06	1.33	0.00	3.25	92.63	94.36	96.56	91.62
				94.1				2.4				1.3							

Table 4 Data from analysis of acetaminophen tablets used for generating control limits for SPC charts for the UV equipment

			For R				For S				FOR X			
LCL	UCL	R	CL	LCL	UCL	S	CL	LCL	UCL	$\bar{X}$	CL	LCL	UCL
0.5295	0.5531	0.0110	0.0115	0.0000	0.0296868	0.0045	0.0049	0	0.0127	0.534	0.5413	0.5317	0.5509
0.5295	0.5531	0.0130	0.0115	0.0000	0.0296868	0.0056	0.0049	0	0.0127	0.5403	0.5413	0.5317	0.5509
0.5295	0.5531	0.0170	0.0115	0.0000	0.0296868	0.0069	0.0049	0	0.0127	0.5387	0.5413	0.5317	0.5509
0.5295	0.5531	0.0250	0.0115	0.0000	0.0296868	0.0104	0.0049	0	0.0127	0.534	0.5413	0.5317	0.5509
0.5295	0.5531	0.0090	0.0115	0.0000	0.0296868	0.004	0.0049	0	0.0127	0.5397	0.5413	0.5317	0.5509
0.5295	0.5531	0.0100	0.0115	0.0000	0.0296868	0.0045	0.0049	0	0.0127	0.5303	0.5413	0.5317	0.5509
0.5295	0.5531	0.0140	0.0115	0.0000	0.0296868	0.0062	0.0049	0	0.0127	0.5393	0.5413	0.5317	0.5509
0.5295	0.5531	0.0110	0.0115	0.0000	0.0296868	0.0048	0.0049	0	0.0127	0.5353	0.5413	0.5317	0.5509
0.5295	0.5531	0.0100	0.0115	0.0000	0.0296868	0.0043	0.0049	0	0.0127	0.537	0.5413	0.5317	0.5509
0.5295	0.5531	0.0090	0.0115	0.0000	0.0296868	0.0037	0.0049	0	0.0127	0.5467	0.5413	0.5317	0.5509
0.5295	0.5531	0.0110	0.0115	0.0000	0.0296868	0.0048	0.0049	0	0.0127	0.5387	0.5413	0.5317	0.5509
0.5295	0.5531	0.0100	0.0115	0.0000	0.0296868	0.0042	0.0049	0	0.0127	0.5377	0.5413	0.5317	0.5509
0.5295	0.5531	0.0140	0.0115	0.0000	0.0296868	0.0062	0.0049	0	0.0127	0.5393	0.5413	0.5317	0.5509
0.5295	0.5531	0.0130	0.0115	0.0000	0.0296868	0.0053	0.0049	0	0.0127	0.5483	0.5413	0.5317	0.5509
0.5295	0.5531	0.0140	0.0115	0.0000	0.0296868	0.0057	0.0049	0	0.0127	0.5413	0.5413	0.5317	0.5509
0.5295	0.5531	0.0100	0.0115	0.0000	0.0296868	0.0043	0.0049	0	0.0127	0.536	0.5413	0.5317	0.5509
0.5295	0.5531	0.0120	0.0115	0.0000	0.0296868	0.0057	0.0049	0	0.0127	0.546	0.5413	0.5317	0.5509
0.5295	0.5531	0.0120	0.0115	0.0000	0.0296868	0.0054	0.0049	0	0.0127	0.5403	0.5413	0.5317	0.5509
0.5295	0.5531	0.0090	0.0115	0.0000	0.0296868	0.0037	0.0049	0	0.0127	0.545	0.5413	0.5317	0.5509
0.5295	0.5531	0.0090	0.0115	0.0000	0.0296868	0.0037	0.0049	0	0.0127	0.546	0.5413	0.5317	0.5509
0.5295	0.5531	0.0100	0.0115	0.0000	0.0296868	0.0042	0.0049	0	0.0127	0.5463	0.5413	0.5317	0.5509
0.5295	0.5531	0.0090	0.0115	0.0000	0.0296868	0.0037	0.0049	0	0.0127	0.543	0.5413	0.5317	0.5509
0.5295	0.5531	0.0110	0.0115	0.0000	0.0296868	0.0048	0.0049	0	0.0127	0.5443	0.5413	0.5317	0.5509
0.5295	0.5531	0.0100	0.0115	0.0000	0.0296868	0.0041	0.0049	0	0.0127	0.5417	0.5413	0.5317	0.5509
0.5295	0.5531	0.0110	0.0115	0.0000	0.0296868	0.0045	0.0049	0	0.0127	0.5373	0.5413	0.5317	0.5509
0.5295	0.5531	0.0090	0.0115	0.0000	0.0296868	0.0042	0.0049	0	0.0127	0.543	0.5413	0.5317	0.5509
0.5295	0.5531	0.0100	0.0115	0.0000	0.0296868	0.0041	0.0049	0	0.0127	0.543	0.5413	0.5317	0.5509
0.5295	0.5531	0.0100	0.0115	0.0000	0.0296868	0.0045	0.0049	0	0.0127	0.5477	0.5413	0.5317	0.5509
0.5295	0.5531	0.0110	0.0115	0.0000	0.0296868	0.0046	0.0049	0	0.0127	0.5493	0.5413	0.5317	0.5509
0.5295	0.5531	0.0120	0.0115	0.0000	0.0296868	0.005	0.0049	0	0.0127	0.5497	0.5413	0.5317	0.5509
		0.011533				0.004928				$\bar{X}$ bar	0.541311		

Table 5 data from 20mg Standard weight used to generate control limits for *s* charts for monitoring the analytical weighing balance

				X				S			
DATA POINTS	B1	B2	B3	$\bar{X}$	CL	LCL	UCL	S	CL	LCL	UCL
1	0.1999	0.2002	0.2001	0.200066667	0.200052222	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
2	0.2001	0.2002	0.1999	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
3	0.2002	0.1999	0.2001	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
4	0.1999	0.2001	0.2002	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
5	0.1999	0.2002	0.2001	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
6	0.2001	0.1999	0.2002	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
7	0.2002	0.2001	0.1999	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
8	0.1999	0.2000	0.2002	0.200033333	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
9	0.2001	0.1999	0.2002	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
10	0.2002	0.2002	0.1999	0.20010	0.200067778	0.199762749	0.200341695	0.000173205	0.000148144	0.0000	0.000380433
11	0.1999	0.2001	0.2001	0.200033333	0.200067778	0.199762749	0.200341695	0.00011547	0.000148144	0.0000	0.000380433
12	0.1999	0.2001	0.2002	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
13	0.2001	0.2002	0.1999	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
14	0.2002	0.1999	0.2001	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
15	0.2001	0.1999	0.2002	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
16	0.1999	0.2002	0.1999	0.2000	0.200067778	0.199762749	0.200341695	0.000173205	0.000148144	0.0000	0.000380433
17	0.1999	0.2001	0.2001	0.200033333	0.200067778	0.199762749	0.200341695	0.00011547	0.000148144	0.0000	0.000380433
18	0.2001	0.1999	0.2002	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
19	0.2002	0.2002	0.1999	0.2001	0.200067778	0.199762749	0.200341695	0.000173205	0.000148144	0.0000	0.000380433
20	0.1999	0.2001	0.2001	0.200033333	0.200067778	0.199762749	0.200341695	0.00011547	0.000148144	0.0000	0.000380433
21	0.2001	0.1999	0.2002	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
22	0.1999	0.2002	0.1999	0.20000	0.200067778	0.199762749	0.200341695	0.000173205	0.000148144	0.0000	0.000380433
23	0.2002	0.1999	0.2001	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
24	0.1999	0.1999	0.2002	0.20000	0.200067778	0.199762749	0.200341695	0.000173205	0.000148144	0.0000	0.000380433
25	0.2001	0.2002	0.1999	0.200066667	0.200067778	0.199762749	0.200341695	0.000152753	0.000148144	0.0000	0.000380433
26	0.2001	0.1999	0.2001	0.200033333	0.200067778	0.199762749	0.200341695	0.00011547	0.000148144	0.0000	0.000380433
27	0.2002	0.1999	0.2002	0.2001	0.200067778	0.199762749	0.200341695	0.000173205	0.000148144	0.0000	0.000380433
28	0.1999	0.2001	0.2001	0.200033333	0.200067778	0.199762749	0.200341695	0.00011547	0.000148144	0.0000	0.000380433
29	0.1999	0.2001	0.1999	0.199966667	0.200067778	0.199762749	0.200341695	0.00011547	0.000148144	0.0000	0.000380433
30	0.2001	0.1999	0.2001	0.200033333	0.200067778	0.199762749	0.200341695	0.00011547	0.000148144	0.0000	0.000380433
			$\bar{X}$	**0.200052222**			$\bar{S}$	**0.000148144**			

Table 6 data from 20mg Standard weight used to generate control limits for *R* charts for monitoring the analytical weighing balance

				X				R			
DATA POINTS	B1	B2	B3	$\bar{X}$	CL	LCL	UCL	R	CL	LCL	UCL
1	0.1999	0.2002	0.2001	0.200066667	0.200052222	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
2	0.2001	0.2002	0.1999	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
3	0.2002	0.1999	0.2001	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
4	0.1999	0.2001	0.2002	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
5	0.1999	0.2002	0.2001	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
6	0.2001	0.1999	0.2002	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
7	0.2002	0.2001	0.1999	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
8	0.1999	0.2000	0.2002	0.200033333	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
9	0.2001	0.1999	0.2002	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
10	0.2002	0.2002	0.1999	0.20010	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
11	0.1999	0.2001	0.2001	0.200033333	0.200067778	0.199769192	0.200335252	0.0002	0.000276667	0.0000	0.000711033
12	0.1999	0.2001	0.2002	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
13	0.2001	0.2002	0.1999	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
14	0.2002	0.1999	0.2001	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
15	0.2001	0.1999	0.2002	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
16	0.1999	0.2002	0.1999	0.2000	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
17	0.1999	0.2001	0.2001	0.200033333	0.200067778	0.199769192	0.200335252	0.0002	0.000276667	0.0000	0.000711033
18	0.2001	0.1999	0.2002	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
19	0.2002	0.2002	0.1999	0.2001	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
20	0.1999	0.2001	0.2001	0.200033333	0.200067778	0.199769192	0.200335252	0.0002	0.000276667	0.0000	0.000711033
21	0.2001	0.1999	0.2002	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
22	0.1999	0.2002	0.1999	0.20000	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
23	0.2002	0.1999	0.2001	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
24	0.1999	0.1999	0.2002	0.20000	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
25	0.2001	0.2002	0.1999	0.200066667	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
26	0.2001	0.1999	0.2001	0.200033333	0.200067778	0.199769192	0.200335252	0.0002	0.000276667	0.0000	0.000711033
27	0.2002	0.1999	0.2002	0.2001	0.200067778	0.199769192	0.200335252	0.0003	0.000276667	0.0000	0.000711033
28	0.1999	0.2001	0.2001	0.200033333	0.200067778	0.199769192	0.200335252	0.0002	0.000276667	0.0000	0.000711033
29	0.1999	0.2001	0.1999	0.199966667	0.200067778	0.199769192	0.200335252	0.0002	0.000276667	0.0000	0.000711033
30	0.2001	0.1999	0.2001	0.200033333	0.200067778	0.199769192	0.200335252	0.0002	0.000276667	0.0000	0.000711033
			$\bar{X}$	**0.200052222**			$\bar{R}$	**0.000276667**			

Declarations

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests
Mercy Okezue (MO) earned her MS and doctorate degree in the BIRS program, Amoreen Naluyima (AN), William Boogore (WB), Emma Kikundwa (EK), Ifudu Collete (IC), and Mukungu Andrew (MA), earned their MS degree in the BIRS program, and are currently Ph.D. students at Purdue University, West Lafayette, Indiana, USA. Stephen Byrn (SB) and Kari Clase (KC) are professors, and academic advisors to the authors in their Ph.D. programs. SB, KC, and Zita Ekeocha (ZE) are team members in the Purdue University BIRS program. Other co-authors work with the NMRAs of Nigeria and Uganda.

The authors declare that they have no conflict of interest.

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Authors' contributions
MO conceived study ideas and collated all data. All co-authors played various roles in analyzing and reporting the results used for the study. KC, SB, and ZE contributed to writing the manuscript. All authors read and approved the final manuscript.

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