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Statistical control of the production of blood components by control charts of attribute to improve quality characteristics and to comply with current specifications

Paulo Pereira[a,*], Jerard Seghatchian[b,*], Beatriz Caldeira[c], Sandra Xavier[d], Gracinda de Sousa[e]

[a] Department of Research and Development, Portuguese Institute of Blood and Transplantation, Avenida Miguel Bombarda 6, 1000-208 Lisbon, Portugal
[b] International Consultancy in Blood Components Quality/Safety Improvement, Audit/Inspection and DDR Strategy, London, UK
[c] Laboratory of Quality Control, Portuguese Institute of Blood and Transplantation, Lisbon, Portugal
[d] Department of Health, Polytechnic Institute of Beja, Beja, Portugal, and Integrated Researcher in NURSE'IN – Nursing Research Unit for South and Islands
[e] Portuguese Institute of Blood and Transplantation, Lisbon, Portugal

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ABSTRACT

Statistical process control (SPC) is closely related to good quality control practices in the manufacturing process. One of the primary goals is to detect unnatural patterns, allowing the production service to control the conformity of the blood components produced. Despite being recommended by national and international standards, its exercise is not uniform, and sometimes the methodology used is misinterpreted as SPC. When the input data has a Gaussian distribution, control charts for variables are proposed. However, when the data distribution is not normal, control charts for attributes are suggested. This article presents and discusses four statistical procedures for the control of attributes using *p*-, *np*-, *u*-, and *c*-charts. An empirical demonstration shows these models are reliable for in routine use in the Blood Establishment quality control, as also suggests the use when the control charts for variables are inapplicable.

1. Introduction

This manuscript follows our previous What's Happening article, where the general principles of statistical process control (SPC) in the production of blood components and control charts for variables are discussed. For a more in-depth understanding of the basic concepts related to the SPC principles and its implementation in a Blood Establishment, the causes of variation, data reliability, and the importance of the normal distribution on the quality control, see [1]. It must be emphasized that the control of the production of blood components is mandatory by The European Directive 2002/98/EC [2] and The European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS) TS111 "Good Practices Guideline" [3]. The TS111 stipulations are included on the 19th edition of The European Directorate for the Quality of Medicines & HealthCare (EDQM) of the Council of Europe guideline (Appendix 4 of [4]). Such requisite is also part of the American Association of Blood Banks (AABB) standards [5].

SPC could be understood as an influential group of problem-solving tools valuable in attaining process stability and improving capability through the decrease of the variability. If a blood component is to meet or exceed specifications, it should be manufactured by a stable or repeatable process. Consequently, the production process must be capable of operating with little variability around the target or nominal dimensions of the quality characteristics of the blood components.

It is noteworthy to mention that the common/natural/expected causes of error are predictable roots of failure mutual to any manufacturing process. In this condition, the special error is higher than what is probable. Therefore, special causes of failure are supposed to happen. The variance and out-of-specification results are considered predominantly in a short-term strategy. The common and special causes are observed in a long-term. The long-standing method is also intended to the constant satisfaction of high-quality specifications, preventing measures and significantly decreasing the products' price. The short-term is associated primarily with the corrective actions, and long-term with opportunities for improvement.

Moreover, specification limits are designated agreeing to the requirements for blood components. The uses of control charts are intended to identify nonconforming lots or individual components and to detect trends. Capability indexes are used to measure and classify the level of production ability to meet the specifications. Hence it should be clear that blood component samples are verified according to requirements, not according to control limits. A manufacturing process is

* Corresponding authors.
E-mail addresses: paulo.pereira@ipst.min-saude.pt (P. Pereira), jseghatchian@btopenworld.com (J. Seghatchian).

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classified as “world class quality” since the attribute results are “on target” with “minimum variance.”

The primary choice of charts in SPC is the control charts for variables. However, since subgroups data is not normally distributed, two alternative strategies are applicable: (a) control charts for variables using normal transformed data or (b) control charts for attributes. In the situation that a characteristic/parameter to be checked cannot be suitably represented numerically, each result is inspected and classified as conforming/nondefective or nonconforming/defective to a specification. This type of characteristics is referred as attributes. For instance, the case of the parameter to be checked in *platelets*, *apheresis*, *leucocyte-depletedin additive solution* is the residual leucocyte count. This measurand distribution is close to a negative binomial distribution (NBD) [6]. On this scenario, the attribute is a characteristic of the number of leucocytes according to a specification: $< 1 \times 10^6$ or $\geq 1 \times 10^6$ per unit, respectively, conforming or not conforming to the EDQM guideline (Component monographs Part C. Platelet components of [4]). Control charts for attributes are recognized as necessary on an SPC strategy as an alternative to the charts for variables. They help to classify areas of production by priorities of improvement, they are essential to administrative processes due to its focus on defects and defective products, and because they distinguish common causes from special causes. Control charts for attributes are applied to determine if the defective product rate is stable and distinguish a deviation from stability in a production process. Several types of control charts are available according to the attributes type and sampling methods. The four main models are considered: *p*-, *np*-, *u*-, and *c*-charts.

Sampling practices suggest testing a representative lot of the manufacturing in controlled conditions consistent with good practices. The proportion is related to full produced blood components for a specified period. Therefore, an appropriate sampling method is needed. The use of inadequate sampling methods could origin biased results followed by biased decisions. It could be applied simple random, systematic, and stratified sampling models [7]. For a more in-depth discussion on sampling models of produced blood components, see [8]. See [9] for further details on SPC applied to the production of blood components.

The focus of this article is the selection and implementation of suitable control charts for attributes as an SPC methodology in a Blood Establishment following current best practices. The cases are from the database of the Quality Control, Portuguese Institute of Blood and Transplantation, Portugal.

2. Material and methods

2.1. Control charts for attributes

The control charts for attributes require a count of a characteristic/attribute of a parameter to be checked (input) instead of an analytical measurement. For instance, the case of the residual leucocyte count checked in *platelets, apheresis, leucocyte-depleted in additive solution*. The classification of attribute results is according to the state of conformity, i.e., no/yes, non-conforming/conforming. Let contemplate *p*-, *np*-, *u*-, and *c*-charts. On a brief introduction, *p*-charts are used to control discrete attribute data. It is intended to control defective and non-defective components in a production process. This chart plots the proportion *p* of the data falling into the relevant category over time using sampling with dimension not fixed. *np*-charts is aversion of the *p*-chart used to control data from a fixed subgroup, i.e., a sample with the same size. The *np*-chart shows the number of occurrences in a category over time rather than the proportion in the category. The actual amount in a category is determined by multiplying the samplesize *n* by proportion *p*. *c*-charts is close to the *np*-chart since both require a fixed number of samples per data point. However, differently, fromthe *np*-charts that represent the proportion data in a specific category, *c*-charts plots count data, i.e., the number of defects/nonconformities. Finally, the *u*-charts, which is a more general version of the *c*-chart oriented to data points that do not come from an equal number of samples. Since the sample sizes are different, the control limits are mobile. Typically, the number of subgroups *m* is ≥ 25, and the number of samples *n* is usually from three to five.

2.1.1. Defective products (nonconform products)

2.1.1.1. p-chart with variable sample size. The center line is equal to the average of the number of process fraction nonconforming *p*. The mathematical model is as follows (entry 7.2 of [10]):

$$\overline{p} = \frac{\sum_{i=1}^{m} D_i}{mn} = \frac{\sum_{i=1}^{m} \hat{p}_i}{m} \tag{1}$$

where a number of nonconforming samples *i*, p_i is the ratio of nonconforming samples *i*, $i = 1, \ldots, m$, *m* is the number of preliminary samples, and *n* is the number of samples of the rational subgroup. *m* should be no less than 20.

The control limits, the upper control limit $UCL_{\overline{p}}$, and the lower control limit $LCL_{\overline{p}}$, are computed using the following models:

$$UCL_{\overline{p}} = \overline{p} + 3\sqrt{\frac{\overline{p}(1-\overline{p})}{n}} \tag{2}$$

where$\overline{p}$is the average of the ratio of nonconforming samples, and *n* is the number of samples of the rational subgroup, and;

$$LCL_{\overline{p}} = \overline{p} - 3\sqrt{\frac{\overline{p}(1-\overline{p})}{n}} \tag{3}$$

2.1.1.2. np-chart with fixed sample size. The center line is equal to the average of the number of the defectives in sampling $\overline{p}$. The model derived from the Eq. (1), as follows (entry 7.2 of [10]):

$$n\overline{p} = \overline{p}(n) \tag{4}$$

where$\overline{p}$is the average of the number of process fraction nonconforming, and *n* is the number of samples of the rational subgroup.

The control limits, the upper control limit $UCL_{n\overline{p}}$, and the lower control limit $LCL_{n\overline{p}}$, are calculated using the following models:

$$UCL_{n\overline{p}} = n\overline{p} + 3\sqrt{n\overline{p}(1-\overline{p})} \tag{5}$$

where$\overline{p}$is the average of the ratio of nonconforming samples, and *n* is the number of samples of the rational subgroup, and;

$$LCL_{n\overline{p}} = n\overline{p} - 3\sqrt{n\overline{p}(1-\overline{p})} \tag{6}$$

2.1.2. Defects (nonconformities)

2.1.2.1. u-chart with variable sample size. The *u* rate mathematical model is as follows (entry 7.2 of [10]):

$$u = \frac{x}{n} \tag{7}$$

where *x* is the number of nonconformities in a sample, and *n* is the number of samples of the rational subgroup.

The center line $\overline{u}$ is equal to the average of the number of process fraction nonconforming *u*.

The control limits, the upper control limit $UCL_{\overline{u}}$, and the lower control limit $LCL_{\overline{u}}$, are computed using the following models:

$$UCL_{\overline{u}} = \overline{u} + 3\sqrt{\frac{\overline{u}}{n}} \tag{8}$$

Where $\overline{u}$ is the observed average number of nonconformities per unit in a initial set of data, and *n* is the number of samples of the rational subgroup, and;

$$LCL_{\overline{u}} = \overline{u} - 3\sqrt{\frac{\overline{u}}{n}} \tag{9}$$

2.1.2.2. c-chart with fixed sample size. The *c* is the number of

nonconformities.The center line $\bar{c}$ is equal to the average of the number of nonconformities c.

The control limits, the upper control limit $UCL_{\bar{c}}$, and the lower control limit $LCL_{\bar{c}}$, are computed using the following models:

$$UCL_{\bar{c}} = \bar{c} + 3\sqrt{\bar{c}} \quad (10)$$

$$LCL_{\bar{c}} = \bar{c} - 3\sqrt{\bar{c}} \quad (11)$$

2.2. Interpreting control charts

The control limits are one of the most critical issues to a robust control chart. The control limits are regarded as trial control limits (entry 6.2.1 of [10]). Moving limits from the center line decrease the chance of type error I, i.e., reduction of the risk of a false out-of-control event (false alarm) since there is no cause. However, this moving will increase the risk of a type II error, i.e., increase the chance the there is happing a true out-of-control event, but it is undetected on the chart. Otherwise, the case the control limits are moved to be closer to the center line, the risk of type I error increases, and the risk of type II decreases. Central line ± 3s corresponds to 0.9973 or 99.73% of the population. Consequently, the probability of type I error is 0.0027 or 0.27 % according to the standard normal table. It could be understood that an incorrect out-of-control or false alarm is made in uniquely 27 out of 10,000 points. Moreover, the probability that point in-control conditions exceed the three-sigma limits in one direction is 0.00135 or 0.14%, reinforcing the need to investigate special causes. Two sets or even three sets of limits could be used. Three-sigma limits are referred as the outer limits, mentioned as action limits. The three-sigma limits are referred as Natural Process Limits, where the data arises from an undisturbed process. Any results out-of-three-sigma, i.e., out-of-control, require an investigation, and a corrective action known as out-of-control-action plan (OCAP), is taken if necessary. Two-sigma and one-sigma are referred as warning limits, and they are useful to identify trends that require an action for improvement to minimize the risk of the production process to be out-of-control. The sample results from the initial subgroups are plotted to verify whether the process was in control when the initial data were reported. Points exceeding the three-sigma limits are inspected. If assignable causes are identified, they are discarded, and new trial control limits are computed.

Since 1956 that the well-established Western Electric rules are used in the industry [11]. They are intended to recognize a sequence of unnatural patterns, increasing the sensitivity for out-of-control events when compared to the single use of the three-sigma rule. Three zones are considered in the application of these rules: A, B, and C. Zone A is between the two-sigma and the three-sigma limit, the zone B is between the two-sigma and one-sigma limit, and zone C is between the two-sigma and the center line. The Western Rules criteria is applied as shown in Table 1 (first four rules). These rules differentiate the process instability including the identification of unnatural patterns by special causes. Table 1 includes a summary of 10 rules to be applied according to the stability of the process. For details about the probability related to the Western Electric rules see [1].

Table 1
A summary of rules for Shewart control charts.

No.	Rule
1	One point out of the three-sigma control limits*
2	Two of three successive points are out of two-sigma warnign limits, but within three-sigma control limits*
3	Four of five sucessive points beyond the one-sigma limits*
4	Eight sucessive points on one side of the center line*
5	Six sucesss points in a row progressively increasing or decreasing (trend)
6	Fifteen points in a row in zone C (both above and below the center line)
7	Fourteen points in a row discontinuous up and down
8	Eight points in a row on both sides of the center line with none in zone C
9	An unusual or nonrandom pattern in the data
10	One or more points near a warning or control limit

Legend: * Western Rules.

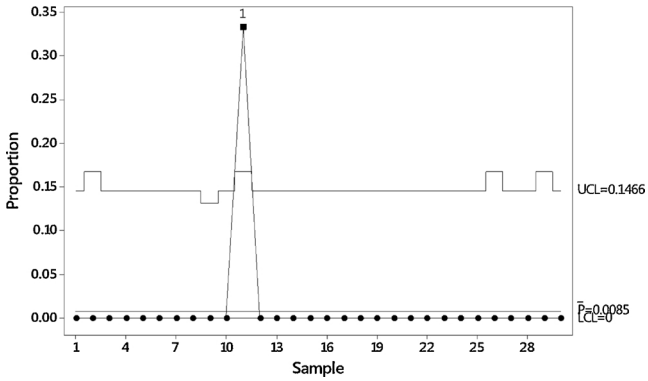

Fig. 1. p-chart for the control of the proportion of residual leucocytes in a sequence of rational subgroups with variable number of samples of *platelets, apheresis, leucocyte-depleted in additive solution.*

It is suggested that the OCAP specifies a complete set of the possible causes to facilitate the diagnostic of the production process. Thinking based on the Pareto principle is recommended. A history of successful OCAP should guide the staff to an easier implementation of next OCAP.

3. Results

3.1. p-chart with a variable sample size

Let consider the residual leucocyte count in a sampling with 30 lots with a fixed quantity of samples per sampling of *platelets*, *apheresis*, *leucocyte-depletedin additive solution.* It is assumed that leucocytes have a nonnormal distribution (NBD [6] or log-normal distribution [12]). A daily lot is manufactured. Sampling is related to the number of blood components produced. p-chart is illustrated in Fig. 1. See Table 2 for input data. Eq. (1) determines the center line, and Eqs. (2) and (3) and the control limits of p-chart chart as follows:

$$\bar{p} = \frac{\sum_{i=1}^{50} D_i}{117} = \frac{1}{117} = 0.0085,$$

$UCL_{\bar{p}} = 0.0085 + 3\sqrt{\frac{0.0085(1-0.0085)}{4}} = 0.1466$, and; $LCL_{\bar{p}} = 0$ (note: since $LCL_{\bar{p}} < 0$, it is assumed to be zero)

3.2. np-chart with a fixed sample size

The previous case is used to the np-chart shown in Fig. 2. See Table 3 for input data. Eq. (4) determines the center line, and Eqs. (5) and (6) and the control limits of np-chart as follows:

$$n\bar{p} = 0.002667(25) = 0.033,$$

Table 2
Residual leucocytes count attributes for 30 lots with a variable number of samples per rational subgroup of *platelets, apheresis, leucocyte-depleted in additive solution.*

No.	n	D_i	$\hat{p}_i$	No.	n	D_i	$\hat{p}_i$	No.	n	D_i	$\hat{p}_i$
1	4	0	0	11	3	1	0.33	21	4	0	0
2	3	0	0	12	4	0	0	22	4	0	0
3	4	0	0	13	4	0	0	23	4	0	0
4	4	0	0	14	4	0	0	24	4	0	0
5	4	0	0	15	4	0	0	25	4	0	0
6	4	0	0	16	4	0	0	26	3	0	0
7	4	0	0	17	4	0	0	27	4	0	0
8	4	0	0	18	4	0	0	28	4	0	0
9	5	0	0	19	4	0	0	29	3	0	0
10	4	0	0	20	4	0	0	30	4	0	0
						$\sum D_i = 1$				$\bar{p} = 0.0085$	

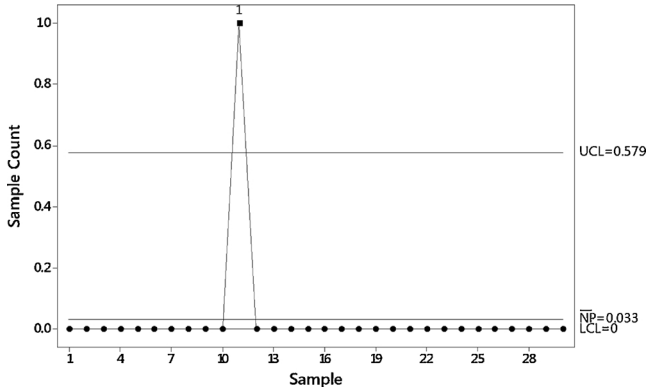

Fig. 2. *np*-chart for the control of the residual leucocytes count of in a sequence of rational subgroups with fixed number of samples of *platelets, apheresis, leucocyte-depleted in additive solution* ($n = 4$).

Table 3
Residual leucocytes count attributes for 30 lots with a fixed number of samples per rational subgroup of *platelets, apheresis, leucocyte-depleted in additive solution*.

No.	n	D_i	$\hat{p}_i$	No.	n	D_i	$\hat{p}_i$	No.	n	D_i	$\hat{p}_i$
1	4	0	0	11	4	1	0.25	21	4	0	0
2	4	0	0	12	4	0	0	22	4	0	0
3	4	0	0	13	4	0	0	23	4	0	0
4	4	0	0	14	4	0	0	24	4	0	0
5	4	0	0	15	4	0	0	25	4	0	0
6	4	0	0	16	4	0	0	26	4	0	0
7	4	0	0	17	4	0	0	27	4	0	0
8	4	0	0	18	4	0	0	28	4	0	0
9	4	0	0	19	4	0	0	29	4	0	0
10	4	0	0	20	4	0	0	30	4	0	0
						$\sum D_i = 1$				$\overline{np} = 0.033$	

$UCL_{n\bar{p}} = 0.033 + 3\sqrt{0.033(1 - 0.0085)} = 0.579$, and; $LCL_{n\bar{p}} = 0$ (note: since $LCL_{n\bar{p}} < 0$, it is assumed to be zero)

3.3. *u*-chart with a variable sample size

The previous case is used to the *u*-chart shown in Fig. 3. See Table 4 for input data. Eq. (7) determines the center line, and Eqs. (8) and (9) and the control limits of *u*-chart as follows:

$\overline{u} = \frac{1}{23} = 0.0431$, $UCL_{\overline{u}} = 0.0431 + 3\sqrt{0.0431(1 - 0.0431)} = 0.3545$, and; $LCL_{\overline{u}} = 0$ (note: since$LCL_{\overline{u}} < 0$, it is assumed to be zero)

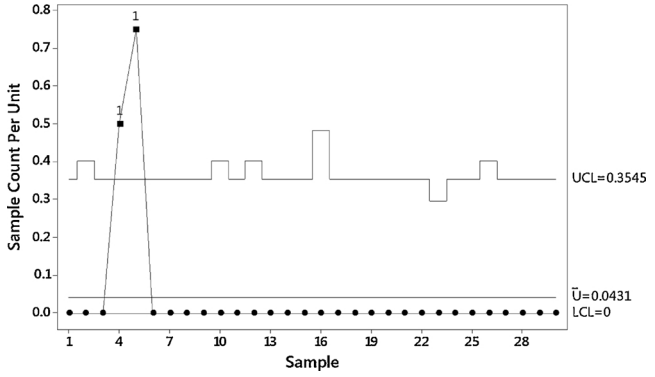

Fig. 3. *u*-chart for the control of the residual leucocytes count per blood component in a sequence of rational subgroups with fixed number of samples of *platelets, apheresis, leucocyte-depleted in additive solution.*

Table 4
Residual leucocytes count attributes for 30 lots with a variable number of samples per rational subgroup of *platelets, apheresis, leucocyte-depleted in additive solution*.

No.	n	D_i	$\bar{u}_i$	No.	n	D_i	$\bar{u}_i$	No.	n	D_i	$\bar{u}_i$
1	4	0	0	11	4	1	0.25	21	4	0	0
2	3	0	0	12	3	0	0	22	4	0	0
3	4	0	0	13	4	0	0	23	6	0	0
4	4	2	0.29	14	4	0	0	24	4	0	0
5	4	3	0.43	15	4	0	0	25	4	0	0
6	4	0	0	16	2	0	0	26	3	0	0
7	4	0	0	17	4	0	0	27	4	0	0
8	4	0	0	18	4	0	0	28	4	0	0
9	4	0	0	19	4	0	0	29	4	0	0
10	3	0	0	20	4	0	0	30	4	0	0
						$\sum D_i = 2$				$\bar{u} = 0.0431$	

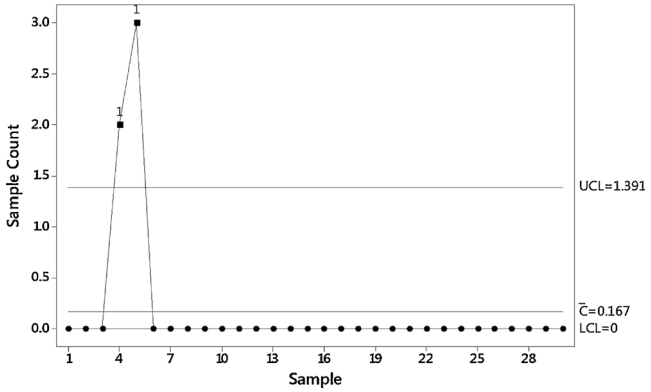

Fig. 4. *c*-chart for the control of the count of residual leucocytes in a sequence of rational subgroups with fixed number of samples of *platelets, apheresis, leucocyte-depleted in additive solution* ($n = 3$).

Table 5
Residual leucocytes count attributes for 30 lots with a fixed number of samples per rational subgroup of *platelets, apheresis, leucocyte-depleted in additive solution*.

No.	n	D_i	c_i	No.	n	D_i	c_i	No.	n	D_i	c_i
1	3	0	0	11	3	1	0.25	21	3	0	0
2	3	0	0	12	3	0	0	22	3	0	0
3	3	0	0	13	3	0	0	23	3	0	0
4	3	2	2	14	3	0	0	24	3	0	0
5	3	3	3	15	3	0	0	25	3	0	0
6	3	0	0	16	3	0	0	26	3	0	0
7	3	0	0	17	3	0	0	27	3	0	0
8	3	0	0	18	3	0	0	28	3	0	0
9	3	0	0	19	3	0	0	29	3	0	0
10	3	0	0	20	3	0	0	30	3	0	0
						$\sum D_i = 2$				$\bar{c} = 0.167$	

3.4. *c*-chart with a fixed sample size

The previous case is used to the *c*-charts shown in Fig. 4. See Table 5 for input data. Eqs. (10) and (11) determine the control limits of *c*-chart as follows:

$\overline{c} = \frac{5}{30} = 0.167$, $UCL_{\overline{p}} = 0.167 + 3\sqrt{\frac{0.167(1 - 0.167)}{4}} = 1.391$, and; $LCL_{\overline{c}} = 0$ (note: since $LCL_{\overline{c}} < 0$, it is assumed to be zero)

All the charts and calculus are computed with Minitab® (Minitab Inc., State College, Pennsylvania, US) software [13].

4. Discussion

For the interpretation of the charts Western Electric rules are applied. Therefore, the *p*-and *np*-charts display one out-of-control result

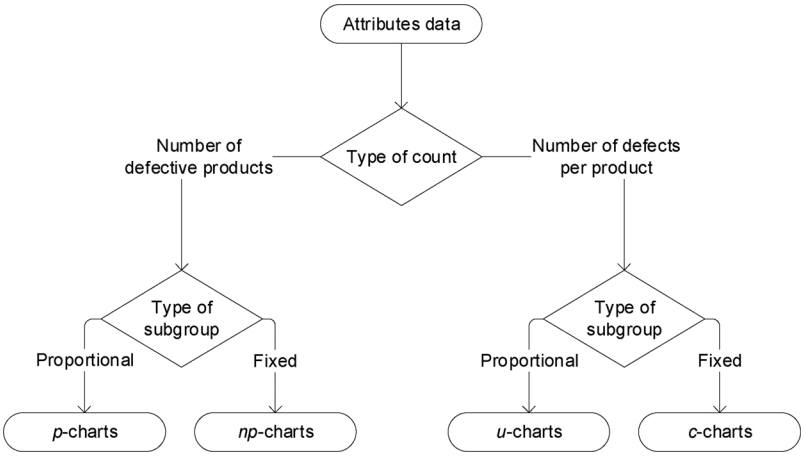

Fig. 5. Selection of the type of chart for attributes.

(lot no. 11). A special cause is detected after an investigation. A whole blood centrifuge is defective. Therefore, an OCAP in the manufacturing process is required. The equipment is out-of-service waiting for successful maintenance. On the next lots, the error is tolerable, for what the OCAP is classified as successful. On the second data set, the *u*- and *c*-charts detected an alarm in the lots no. 4 and 5. A special cause is identified. A lack of skills by one new technician is recognized. OCAP is applied and is classified as successful after lot no. 6.

The robustness of control decision is not related only to the statistical model, but could also be associated with the data distribution and outliers. Anytime the distribution should be verified; we suggest the D'Agostino K-squared test [14] for the examination of the underlying distribution of a random variable normally distributed. See [1] for details on its application to blood components data. Moreover, the decision reliability is also dependent on the trueness of the data. On this perspective, another main concern is to input outliers [15] to the attributes computations. Consequently, the staff should implement a method to assure the detection and correction/deletion of outliers. A particular outlier could cause a false attribute (biased attribute). As a good practice, it is suggested the use of statistical tests such as the Grubbs test [16], the Generalized Extreme Studentized Deviate (ESD) test [17], or the Tukey test [18] if it is suspected more than one outlier. Alternatively to a statistical verification, the use of a pair of analysts to review the input data is strongly advised. For further details on the application of these tools to the control of blood components see [1].

Furthermore, common causes of variation such as the biological variation should also be clearly understood to recognize performance characteristics of specific productions. Blood components manufacturing process $f(x)$ has a repeatable value making a sequence of activities transforming inputs x into reproducible outputs y. The outcome is permanently influenced by a variation, including common causes of variation ("background noise"). Since what is processed is human blood components, there is always the influence of the biological variation to the testing parameters, such as the number of leucocytes. It could be interpreted as a significant variation component that cannot be corrected (a common cause of variation) and should be considered on the discussions when the production process has a systematic low capability index in stable conditions [19]. Note that the biological variation is not common in most of the industry where the full critical production variables are controlled. The biological variation is associated with inter-individual (between-subject) and intra-individual (within-subject) sources [20]. Other common causes arise from people, environment, methods, materials, measures, and equipment in controlled conditions. Variability larger than the "background noise," regularly signifies an intolerable level of process performance. The associated sources of variability are referred as "assignable causes of variation." A process that is operating in the presence of assignable causes is said to be an "out-of-control process." Reducing the common causes of variation is a challenge that should be understood as possible, but it can never be removed.

Root-cause analysis, correction, and CAPA are applicable (entry 10.2 of [21]) to identify and correct special causes. The most complicated processes require increased effort to determine the root-cause for exceptional causes. The consistency of the production and waste on the budget could occur in the cases a special cause is not detected or if there is a false rejection of lots due to false alarms, respectively.

The attributes charts are designated to reduce the process fallout. They add value to the evaluation of multiple step processes, and they are an alternative when variables are unmeasurable. Their role is also significant to perform a historical synopsis of the manufacturing process. Additionally, they have advantages, such as the low-priced cost of inspection due to requiring a smaller number of samples and because it is a simpler method compared to the control for variables. Despite the control for attributes to be intended to enhance the processes continuously, it is less effective than control for variables to decrease the variance, to control and report the stability of the operations, to follow-up the methods, to determine the procedure performance, and to identify non-conformities about lot specifications at an early stage. Control charts for attributes are not so advantageous to locate the special causes due to be uniquely acknowledged the number or ratio of results rejected in sampling. Likewise, the risk of accepting non-conforming products is substantially higher. It is due to the fact that some rules are regularly verified in a high number of samples for which the control is sometimes retrospective. Fig. 5 displays a diagram to select the chart per type. Note that the use of the control charts should be a compliment on an SPC strategy by the other six statistical tools of the "magnificent seven" whenever appropriate: (1) histogram or stem-and-leaf plot; (2) check sheet; (3). Pareto chart; (4) cause-and-effect diagram; (5) defect concentration diagram, and; (6) scatter diagram. These problem-solving tools should be recognized throughout the production and quality control services. Its application able the Blood Establishment to identify also opportunities for improvement and to assist in reducing the variability, eliminating waste, and improving the production process complementing cycles such as DMAIC (an acronym for Define, Measure, Analyze, Improve and Control) on a Six Sigma manufacturing policy [22].

In short, this article demonstrates that the implementation of control charts for attributes is an essential tool to control the production as part of an SPC strategy. The theory and cases presented are intended to support the laboratorian to understand the essential principles of these type of charts based on real examples. Nevertheless, the efficient application of the control charts for attributes depends on the competences of the personnel. Our Blood Establishment experience recommends as a first step to receive the support of a consultant and in a

second stage to start the formation of a technician to be the head to maintain and improve the SPC procedure.

References

[1] Pereira P, Seghatchian J, Caldeira B, Xavier S, Sousa G. Statistical methods to the control of the production of blood components: principles and introduction to control charts for variables. Transfus Apher Sci 2018;57(1):132–42.
[2] Commission directive 2002/98/EC of the European parliament and of the council as regards setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending directive 2001/83/EC. Off J Eur Union 2018;L33:30–40.
[3] European directorate for the quality of medicines & health care of the council of Europe (EDQM/CoE). TS111 good practice guidelines (for blood establishments). European Committe (Partial Agreement) on Blood Transfusion. EDQM; 2017.
[4] European directorate for the quality of medicines and health care. Guide to the preparation, use and quality assurance of blood components. 19th ed. Strasbourg: EDQM; 2017.
[5] American association of blood banks. Standards for blood banks and transfusion services. 31th ed. Bethesda (MD): American Association of Blood Banks; 2018.
[6] Finch SJ, Chen JB, Chen CH, Hall MM, Matkovich V, Wenz B, et al. Process control procedures to augment quality control of leukocyte-reduced red cell blood products. Stat Med 1999;18(10):1279–89.
[7] Thompson SK. Sampling. 3rd ed. New York (NY): John Wiley and Sons, Inc.; 2012.
[8] Pereira P, Seghatchian J, Caldeira B, Santos P, Castro R, Fernandes P, et al. Sampling methods to the statistical control of the production of blood components. Transfus Apher Sci 2017;56(6):914–9.
[9] Pereira P. Statistical control of the production of blood components using variables and attributes charts, and capability indexes. In: Luna A, editor. Blood donations: attitudes, safety and future directions. Hauppauge (NY): Nova Science Publishers; 2016. p. 27–72.
[10] Montgomery D. Introduction to statistical quality control. 7th ed. New York (NY): John Wiley and Sons, Inc.; 2012.
[11] Statistical quality control handbook. 2nd ed. Western Electric Company, Inc.; 1958.
[12] Dumont L, Dzik W, Rebulla P, Brandwein H. Practical guidelines for process validation and process control of white cell-reduced blood components: report of the Biomedical Excellence for Safer Transfusion (BEST) working party of the International Society of Blood Transfusion (ISBT). Transfusion 1996;36(1):11–20.
[13] Minitab v.18.1. State College (PA): Minitab, Inc.; 2017.
[14] D'Agostino R. Transformation to normality of the null distribution of g1. Biometrika 1970;57(3):679–81. http://dx.doi.org/10.1093/biomet/57.3.679.
[15] International Organization for Standardization. ISO 16269 statistical interpretation of data – part 4: detection and treatment of outliers. Geneva: ISO; 2010.
[16] Grubbs F. Procedures for detecting outlying observations in samples. Technometrics 1969;11(1):1–21.
[17] Rosner B. Percentage points for a generalized ESD many-outlier procedure. Technometrics 1983;25(2):165–72.
[18] Tukey J. Exploratory data analysis. Reading (MA): Addison-Wesley Publishing Company; 1977.
[19] Bissell AF. How reliable is your capability index? Appl Stat 1990;39(3):331–40.
[20] Fraser C. Biological variation: from principles to practice. Washington (DC): AACC Press; 2001.
[21] International Organization for Standardization. ISO 9001 quality management systems – requirements. 5th ed. Geneva: ISO; 2015.
[22] George ML. Lean six sigma for service. New York (NY): McGraw-Hill; 2003.