Application of Statistical Process Control (SPC) in the Quality Control Monitoring of Blood Products

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Introduction and Purpose

The use of statistical methods (including statistical process control, SPC) for monitoring quality of blood components is a requirement of EU Directives (2002/98/EC, 2004/33/EC) and of the "Guide to the Preparation, Use and Quality Assurance of Blood Components" (16th Edition 2010, Chapter 1, Paragraph 11). However, practical advice is lacking in these sources. Beckman et al. (Transfusion Medicine, 2009, 19,329-339) provide in their article a practical approach for applying SPC to blood component production. The "process capability" (Cpk) is one important index to judge and predict if a process is reliably capable to meet the specifications. We use this Cpk-index for the evaluation and monitoring of our quality control (QC) data.

Methods

All methods presented here are according to Beckman et al. (Transfusion Medicine, 2009, 19, 329-339) and the methodology is only applicable on variable data which are normally distributed (or transformed to almost normal distribution). In addition, specification limits have to be defined to calculate the Cpk index as follows:

Cpk = (USL-X)/3SD and/or Cpk = (X-LSL)/3SD

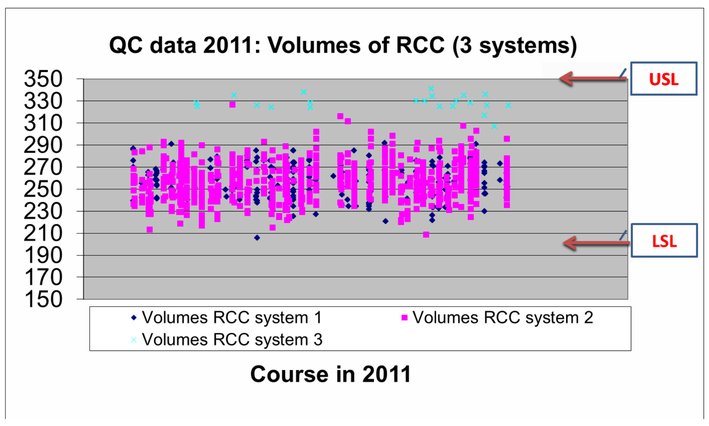
X = mean; SD = standard deviation;
USL = upper specification limit; LSL = lower specification limit

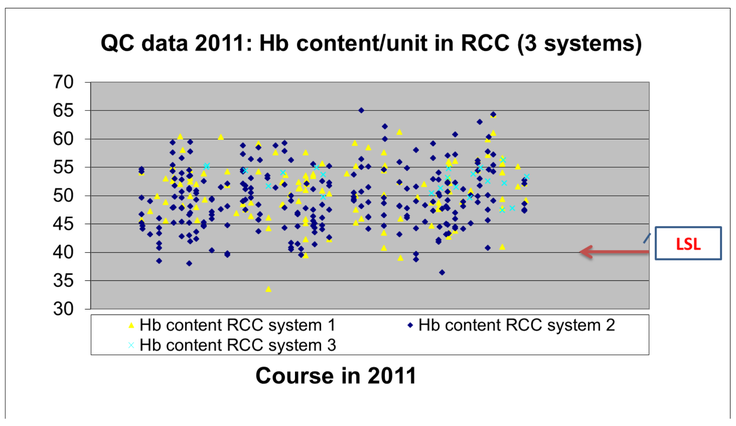
The Cpk indicates how well the distribution of data fits within the specification limits and how well the data are centred about the nominal (target) value. When using two specification limits (USL and LSL), the lower Cpk value is used as Cpk index (where X is closer to the specification limit). The larger the value of Cpk, the better the process is predicted to perform in meeting specifications. Cpk values can be used to predict the level of non-conformity as shown in table 1. By assessing a criticality (low, medium, high) for each parameter under consideration, Cpk bandings can be used to classify the conformity of the processes (capable, borderline, incapable).
This is shown in table 1. In general, a process is regarded as highly capable if Cpk is >1.40.

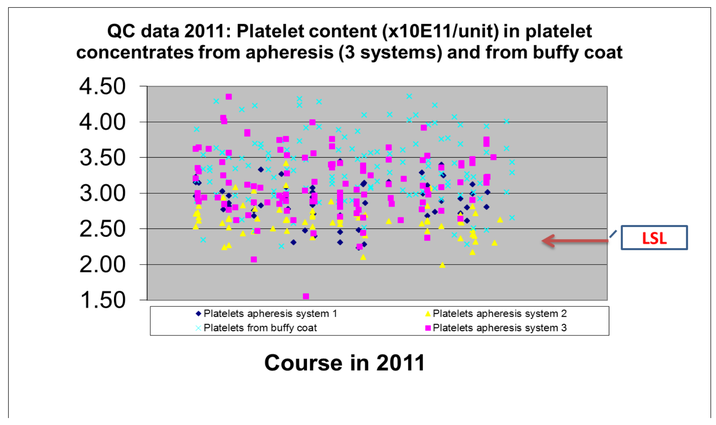
Table 1

Specification type	Cpk values						
Two sided	>1.47	1.30–1.46	1.10–1.29	0.86–1.09	0.54–0.85	0.39–0.53	<0.39
One sided	>1.40	1.23–1.39	1.03–1.22	0.77–1.02	0.43–0.76	0.21–0.42	<0.21
% Non-conformity	< 0.001	0.001–0.01	0.01–0.1	0.1–1.0	1.0–10	10–25	>25
Parameter Criticality	Cpk banding						
High	Capable		Borderline	Incapable			
Medium	Capable				Borderline	Incapable	
Low	Capable					Borderline	Incapable

Results







Figures 1-3 show the data of three different QC parameters in the course of 2011. USL and LSL indicate upper and lower specification limits of the products.
Figure 1: Volumes of Red Cell Concentrates (RCC), 3 different collection and production systems
Figure 2: Haemoglobin content per unit in RCC, 3 different collection and production systems
Figure 3: Platelet content (x10E11/unit) in platelet concentrates from apheresis (3 different collection procedures) and platelets from buffy coat

This looks good! But: Is it good? Is each process capable? Are the processes different?

Table 2 Cpk values for RCC 2011	RCC System 1		RCC System 2		RCC System 3	
Parameter	Hb content/unit	Volume	Hb content/unit	Volume	Hb content/unit	Volume
Cpk	0.70	1.21	0.56	1.04	1.76	3.39
% non conformity predicted	1.0-10%	0.01-0.1%	1.0-10%	0.1-1.0%	< 0.001%	<0.001%
% non conformity observed	2.5%	0%	1.6%	0%	0%	0%
Criticality	medium	low	medium	low	medium	low
Cpk banding	borderline	capable	borderline	capable	capable	capable

Table 2 shows the Cpk values for the parameter "volume" and "Hb content/unit" in three different RCC systems. The process is considered as borderline for the Hb content in systems 1 and 2. The predicted rates of non-conformity (1-10%) are consistent with those observed (2.5%, 1.6%) and this is still compliant with the specifications of B-CH SRC (tolerated non-conformity rate of 10%).
For all other parameters, the processes are capable with a very low probability of non-conformity. System 3 is clearly superior to systems 1 and 2, where there is still room for improvement (at least regarding the mentioned parameters).

Table 3 Cpk values for platelets (after Intercept treatment) 2011	Platelets Apheresis System 1	Platelets Apheresis System 2	Platelets Apheresis System 3	Platelets from buffy coat	All platelets
Parameter	Platelet content/unit	Platelet content/unit	Platelet content/unit	Platelet content/unit	Platelet content/unit
Cpk	0.56	0.30	0.54	0.66 (2012: 0.71)	0.46 (2012: 0.54)
% non conformity predicted	1.0-10%	10-25%	1.0-10%	1.0-10%	1.0-10%
% non conformity observed	8.6%	14.5%	3.5%	2.3%	5.9%
Criticality	medium	medium	medium	medium	medium
Cpk banding	borderline	incapable	borderline	borderline	borderline

Table 3 shows the Cpk values and the judgement for the parameter "platelet content/unit" in three different apheresis procedures, in buffy coat platelets and for all platelets together. All but one processes are considered as borderline, system 2 is judged incapable. Again, the predicted non-conformity rates are consistent with those observed and -except for system 2- they are still compliant with the specifications of B-CH SRC (tolerated non-conformity rate of 10%). This evaluation also allows a comparison among the different procedures and it showed a clear need to improve the platelet yield of the apheresis procedures. The settings of the instruments were therefore adjusted in 2012 and preliminary data already show positive effects.

Conclusions

The Cpk index is a valuable tool to objectively assess the goodness of a process, but also for recognizing trends in QC data. The index is especially useful to compare different manufacturing techniques leading to the same end product. This can be useful in the evaluation of different techniques or for quality monitoring of established processes.

Swiss Transfusion 2012, Jahrestagung B-CH SRK/SVTM, Basel