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SHORT RUN CONTROL CHARTS AS AN INTERNAL QUALITY CONTROL TOOL

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Abstract – A novel methodology based on short run control charts was developed to establish simultaneous intra and inter daily control of instrumental blank samples for trace elements analysis through inductively coupled plasma mass spectrometry (ICP-MS). Eleven inorganic trace elements were analyzed, where chromium was selected to illustrate the methodology. The use of joint control charts, both based on the Quesenberry Q-statistics, revealed to be a suitable tool in detecting possible instrument contaminations as well as evaluating IPC-MS stability.

Keywords: ICP-MS, instrumental blank samples, trace elements, contamination, short run control chart.

1. INTRODUCTION

Inductively coupled plasma mass spectrometry (ICP-MS) is one of the most suitable analytical techniques to quantify inorganic components at trace concentrations, i.e., expressed in at the µg/ kg level [1, 2].

Internal Quality Control (IQC) is one of the most challenging aspects in ICP-MS analysis due to the wide number of analytes and matrixes associated with sample preparation methods. ICP-MS analysis requires the previous definition of quality assay and performance criteria in order to obtain rigorous analytical procedures [3].

Statistical quality control approach, such as control charts based on Shewhart principles, have been gaining a relevant importance in the activity of IQC, since this must be performed in a daily quality control of routine analytical work. According to Ríos et al. [4] IQC is a key activity within a Quality Assurance (QA) system, where the use of control charts should be an indispensable tool. The basic principles of control charts, with useful guidelines and examples, are well explained in three important ISO standards [5-7], and complemented with the IUPAC Harmonized Guidelines for IQC [8]. Ríos et al. [4] expanded the use of the Shewart control charts to qualitative analysis applied to blank samples. Thompson and Magnusson [9] and Simonet [10] present more applications of control charts in the context of IQC. The first one used a multiple univariate control charts to monitor surrogate control materials and univariate charts to test duplicates, whereas the second one used univariate control charts to monitor blank samples in a qualitative base.

Experimental blank samples are usually implemented in a daily routine to evaluate the equipment's background and to discriminate between chemical contaminants originated from matrix and those resulted from laboratory. Limit of detection (LOD) and limit of quantification (LOQ) are the crucial metrological concepts addressing these concerns [11]. LOD is defined as the lowest amount or concentration of an analyte in a sample, which can be reliably detected, but not necessarily quantified. LOQ is the lowest amount or concentration of an analyte in a sample that can be reliably quantified with an acceptable level of precision and accuracy [1, 2, 12].

Despite LOD and LOQ being relevant criteria in the analysis of contaminants, there is a lack of information about the best approach to estimate them due to their quantification at very low amounts.

The main goal of this work is to evaluate the suitability of a methodology based on a special case of statistical control charts, specifically the Short Run Control Charts. Based on the Q-statistic developed by Quesenberry [13], a joint control chart was established for an intra and inter day instrumental blank sample control, for monitoring and assessing the statistical consistence of the blank data in a daily routine.

This methodology was applied as the first step for Quality Control framework during the quantification of eleven inorganic trace elements (Pb, Cr, Mn, Co, Ni, Cu, Zn, As, Se, Sr and Cd) by ICP-MS, in a diverse set of matrixes (rice, cork stopper, quinoa, pear-apple, tomato, canned crab, tartaric acid, corn and honey).

2. MATERIALS AND METHODS

2.1. Samples preparation

All samples and standard preparation steps were carried out in clean room facilities.

Blank samples were prepared on a daily basis by preparing a solution of nitric acid (2%V/V) in Milli-Q water (18 µΩ) (Q-POD Millipore, Interface, Portugal).

A nitric acid solution with a 2–4% concentration was also used for working standards, diluting samples and as rinsing solution between samples for the ICP-MS. Internal standards

were added to all samples and working standards in order to correct for instrumental drift.

2.2. Reagents

All reagents were of high analytical grade. All solutions were prepared using ultrapure water (18.2 MΩ cm) (Q-POD Millipore, Interface, Portugal) and Nitric acid pro analysis (65% v/v) (Merk, VWR, Portugal) was previously purified by sub-boiling distillation using a SubPur apparatus (Milestone, Unicam, Portugal). Hydrogen peroxide solutions acquired were of ultrapure grade.

For the calibration curve working multi-element standard solutions were prepared from mono-element high purity ICP stock standards containing 1000 mg/L of each element.

Internal Quality Control standard solutions were prepared using the multi-element standard solution, high purity ICP 100 mg/L, from Merck (21 elements diluted in nitric acid) containing all the elements under study.

According to the matrix under analysis internal standards were chosen between Yttrium, Indium and/or Rhodium (1000 mg L^{-1}; Merck).

2.3. Instrumentation

Measurements were performed using a quadrupole inductively-coupled plasma mass spectrometry (ICP-MS; Thermo Elemental, X-series 2, UK).

ICP-MS tuning was performed on a daily basis with a diluted 10 mg L-1 multi-element solution (Analytika, UNICAM, Portugal). Operating conditions for ICP-MS were for experience, optimized as follows:

- Extraction: -113.7, 190
- Focus: 10.0
- Pole Bias: -0.1
- Hexapole Bias: -3.0
- Nebulizer flow rate: 0.87 L min-1
- Forward Power: 191 1404 W
- Cool gas flow rate: 13.0 L min-1
- Auxiliary gas flow rate: 0.90 L min-1
- Sampling Depth: 120, 192
- Standard Resolution: 135
- High Resolution: 150
- Analogue Detector: 1902
- PC Detector: 3353.

The parameters were monitored daily for elementary stability and sensitivity, mass calibration and for the presence of oxides and doubly charged ions, and the above conditions optimized accordingly.

3. PROPOSED METHODOLOGY

The use of quality control charts to monitor and evaluate statistical consistency of instrumental blank samples can constitute a powerful tool in IQC. However, special care must be taken regarding the number of collected samples and subsequent sampling parameters estimation.

The proposed methodology, presented in Fig. 1, contemplates intra-day (on-line) and inter-day (off-line) control charts.

Both situations (intra and inter day) have in consideration the lack of significant information regarding the sample size. The first application allows the monitoring and control of individual instrumental blank values, obtained during a working day, allowing the detection of possible contaminations in the ICP-MS measurement process. The second application allows the monitoring and evaluation of blank data statistical consistency (daily instrumental blank mean) in a retrospective point of view.

The main steps of the proposed methodology can be summarized in: preliminary analysis, intra-day control and inter-day monitoring.

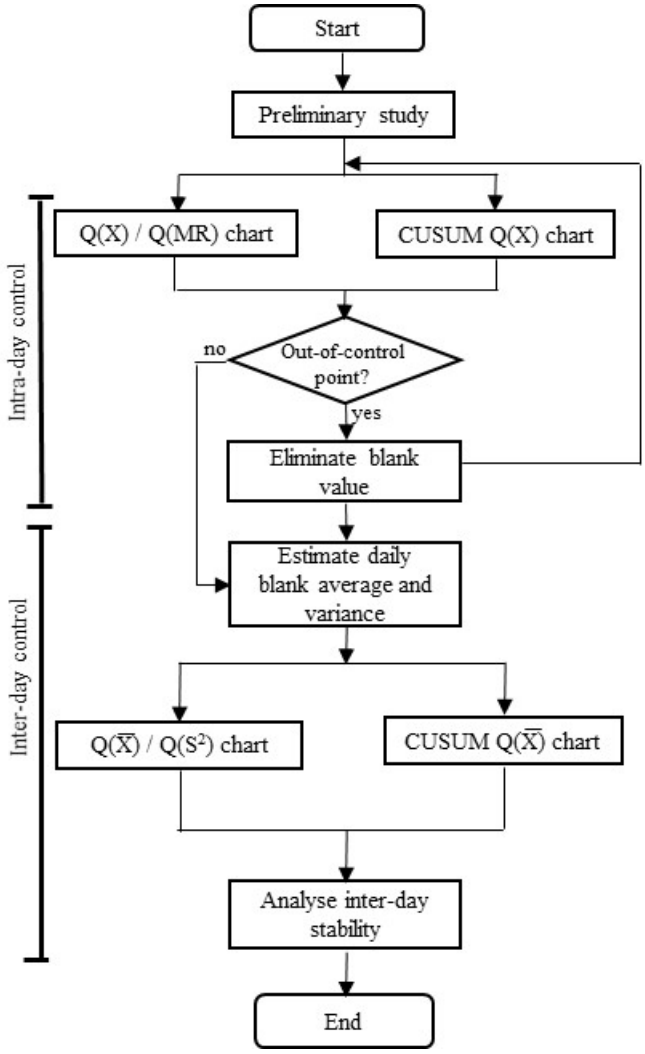

Fig. 1. Proposed Methodology.

3.1. Preliminary analysis

Whenever historical data is available, a preliminary study should be conducted envisaging a better knowledge of the process under study. A graphic study of the data should be accomplished as a starting point, followed by a careful outlier study, and completed with statistical inference studies.

One-way and/or two-way analysis of variance (ANOVA) can be applied using a set of days and/or the elements under study as factors. This ANOVA study will allow the evaluation of inter-day consistency and therefore signaling any element that needs further attention. The ANOVA assumptions should not be neglected, i.e. residuals with null mean and constant variances (homoscedasticity), normally and independently distributed. If normality or homoscedasticity is violated, than a non-parametric approach should be used, such as the Kruskal-Wallis test.

3.2. Intra-day control – Q(X) / Q(MR) and CUSUM Q(X) Charts

Knowing that an auto-test is made to the equipment at the beginning of each day, with no more than 15 instrumental blank samples collected, the blank measurements at ICP-MS is characterized as a starting-up process.

The limited number of observations gathered in each day does not allow a satisfactory blank in-control parameter estimation. This situation can be overcome through Quesenberry Q-statistics [13], initially developed for short run or batch processes, where the phase I of statistical process control is not present [13, 14]. The Q-statistic, denoted by $Q_r(X_r)$, is obtained by (1):

$$Q_r(X_r) = \Phi^{-1}\left(G_{r-2}\sqrt{\frac{r-1}{r}}\left(\frac{X_r-\bar{X}_{r-1}}{S_{r-1}}\right)\right),\ r = 3, 4, \ldots \quad (1)$$

where X_r is the blank value at r instance, Φ^{-1}denote the inverse of the standard normal distribution function, G_ν is the t-student distribution with ν $(r-2)$ degrees of freedom, $\bar{X}_{r-1}$ and S_{r-1} corresponds, respectively, to the average and standard deviation of the $(r-1)$ last observations. Once collected the second blank sample, a Q(X) chart can be initiated, with upper and lower control limits at 3 and -3, respectively. This control chart allows detecting moderate to large shifts in blank samples. As an approximation to control the variability, this chart is usually followed by a $Q_r(MR_r)$ chart, where *MR* corresponds to the instrumental blank samples moving range, given by $|X_r - X_{r-1}|$. The Q-statistic for the moving range - $Q_r(MR_r)$ – is obtained by (2):

$$Q_r(MR_r) = \Phi^{-1}\left(F_{1,\nu}\left(\frac{\nu(MR)_r^2}{MR_2^2+MR_4^2+\cdots+MR_{r-2}^2}\right)\right), \quad (2)$$

$r = 4, 6, \ldots$

where $F_{1,\nu}$ is the Fischer distribution with $r/2-1$ degrees of freedom. Once at the third blank sample, the chart can be initiated, also with upper and lower control limits at 3 and -3, respectively.

When the daily sample size is considerably reduced, the use of a moving range chart Q(MR) can be dispensed, since only $r/2-1$ values are available to be plotted in the chart, due to the fact that the benefit/effort ratio is inefficient.

A combined control is suggested with the CUSUM Q(X), increasing blank sample trend detection efficacy since contamination can be progressive. CUSUM Q(X) control chart can be easily obtained by (3) and (4), after definition of the reference value k and the control limit h [13, 14].

$$T_t = min\big(0, T_{t-1} + (Q_t + k)\big) \quad (3)$$

$$C_t = max\big(0, C_{t-1} + (Q_t - k)\big) \quad (4)$$

with $T_0 = 0$ and $C_0 = 0$, where if $T_t < -h$ or $C_t > h$ than a decrease or increase in the parameter is signalled, respectively.

3.3. Inter-day control – Q($\bar{X}$) / Q(S^2) and CUSUM Q($\bar{X}$) Charts

Similarly to intra-day control, a double control was proposed with Q($\bar{X}$) / Q(S^2) and CUSUM Q($\bar{X}$) charts to monitor instrumental blank stability along the days. For Q($\bar{X}$) and Q(S^2) charts the statistic can be computed by (5) and (6), respectively:

$$Q_i(\bar{X}_i) = \Phi^{-1}\left(G_{n_1+\cdots+n_{i-1}}(\omega_i)\right),\ i = 2, 3, \ldots. \quad (5)$$

$$Q_i(S_i^2) = \Phi^{-1}\left(F_{n_{i-1},n_1+\cdots+n_{i-1}-i+1}(\theta_i)\right),\ i = 2, 3, \ldots. \quad (6)$$

where F_{ν_1,ν_2} is the Fischer distribution with $\nu_1 = n_{i-1}$ and $\nu_2 = n_{i-1} - i + 1$ degrees of freedom.

The parameters ω_i and θ_i are given, respectively by (7) and (8).

$$\omega_i = \sqrt{\frac{n_i(n_1+\cdots+n_{i-1})}{n_1+\cdots+n_i}}\left(\frac{\bar{X}_i-\bar{\bar{X}}_{i-1}}{S_{p,i-1}}\right),\ i = 1, 2, 3, \ldots \quad (7)$$

$$\theta_i = \frac{(n_i+\cdots+n_{i-1}-i+1)S_i^2}{(n_1-1)S_i^2+\cdots+(n_{i-1}-1)S_{i-1}^2},\ i = 1, 2, 3, \ldots \quad (8)$$

In (7) $\bar{X}_i$ is the average of the blank sample i and in (8) S_i^2 is the variance of the blank sample. $\bar{\bar{X}}_{i-1}$ and $S_{p,i-1}^2$ are the average and the combined variance of the $(i-1)$ blank samples, respectively obtained by (9) and (10).

$$\bar{\bar{X}}_{i-1} = \frac{n_1\bar{X}_1+\cdots+n_{i-1}\bar{X}_{i-1}}{n_1+\cdots+n_{i-1}} \quad (9)$$

$$S_{p,i-1}^2 = \frac{(n_1-1)S_1^2+\cdots+(n_{i-1}-1)S_{i-1}^2}{n_1+\cdots+n_{i-1}-i+1} \quad (10)$$

The control limits are fixed at 3 and -3 for both mean and variance control charts.

Regarding CUSUM Q($\bar{X}$), once defined the reference value k and the control limit h, the parameters T_t and C_t can be obtained by (3) and (4), respectively, considering as Q_t the Q($\bar{X}$) values obtained by (5).

Contrarily to the intra-day control scheme, where the benefit/effort ratio can be reduced, especially if the daily sample size is small, using a Q(S^2) chart conjoint with the Q($\bar{X}$) and the CUSUM Q($\bar{X}$) charts will allow detection of significant increases in the blank variability that may occur in specific days, that does not correspond to a mean shift or trend.

4. RESULTS AND DISCUSSION

4.1. Preliminary analysis

Two sets of data were collected during 2013 and 2014. Data from six and seven days was collected, respectively in the first and second years. The days were selected in such a way that they do not respect to consecutive days of both years and a special care was taken with the total number of instrumental blanks collected in each day (sample size ranged from 4 to 7).

A graphical analysis, followed by an outlier study was performed, with no outliers identified. A two-way ANOVA were applied, through which was possible to demonstrate the existence of significant differences not only between the eleven trace elements in study (Pb, Cr, Mn, Co, Ni, Cu, Zn, As, Se, Sr, Cd) but also between days (p-value < 0.05). This result was consistent for the two set of data, evidencing the need to control and monitor blank samples intra-day and inter-day behavior in a routine basis. All ANOVA assumptions were checked against any violation conditions in what respects to both sets of data.

4.2. Intra-day control – Q(X) and CUSUM Q(X) Charts

A new set of twelve days pertaining to the last half of 2014 was considered for this study, where in each day the number of instrumental blanks varied between 7 and 12 samples. Chromium (Cr) was the trace element chosen, where the twelve days are shown in Figs. 2, 3 and 4, respectively for Q(X), Q(MR) and CUSUM Q(X) charts.

A joint control chart analyses allows to identify two out-of-control occurrence at day 4 sample 6 and day 11 sample 4 in Q(X) chart and one out of control at day 4 but sample 8 in CUSUM Q(X). The two out-of-control data event at day 4 indicates that an increase in the Cr blank value occur (chart Q(X)), signaling the need for intervention over the ICP-MS analyses, whereas CUSUM Q(X) shows a trend in the blank values, meaning the persistence of a high tendency of Cr in blanks. The second out of control on Q(X) chart at day 11 sample 4 evidences a shift in an isolated sample, followed by a significant decrease in the blank values.

A different situation occurred at the end of the first day, evidenced by a decrease trend in Cr blank values (Fig. 4). Although this occurrence means an out-of-control situation, it corresponds to smaller blank values, as expected.

Regarding the Q(MR) chart no out of control was detected, despite the sample 6 of the day 4 is located above the warning limits (at two standard deviation of the center line - 2).

4.3. Inter-day control – Q($\bar{X}$) and CUSUM Q($\bar{X}$) Charts

At the end of the day all out-of-control values must be eliminated from the daily blank sample mean and variance, in accordance with the methodology proposed in Fig. 1.

Figs. 5, 6 and 7 shows Q($\bar{X}$), Q(S^2) and CUSUM Q($\bar{X}$) charts for chromium, where twelve daily instrumental blank sample means and variances are represented through Q-statistics.

Joint analysis signals an out-of-control occurrence focused at the fourth and fifth days at Q(S^2) chart, denoting an increase in data dispersion, followed by two out of controls at the fifth and the sixth days at CUSUM Q(X) chart, which is also well characterized through higher blank means in three consecutive days (days 3, 4 and 5) in Q($\bar{X}$) chart. After the sixth day instrumental blank means and variances decreased significantly, inclusively with Q(S^2) values plotted below the lower control limit. This evidence denotes a well-established IQC, however more daily data should be included to continuously update the parameters and improve its estimative.

5. CONCLUSIONS

The use of control charts in IQC context, applied in a daily basis to instrumental blank monitoring in IPC-MS, revealed to be a useful tool. This analysis allows the detection of abnormal conditions throughout a day (intra-day control), as well as assessing instrumental blanks statistical consistency between different days (inter-day monitoring).

The combination of Q (observation/mean and moving range/variance) and CUSUM Q charts revealed to be a valuable tool since joint analysis increases the sensitivity in the detection of shifts and trends in data, as well as increases in data variability.

Q-statistic has allowed to overcome two important conditions, namely the lack of sufficient samples for process parameter estimation and the fact that sample size may not remain constant between days.

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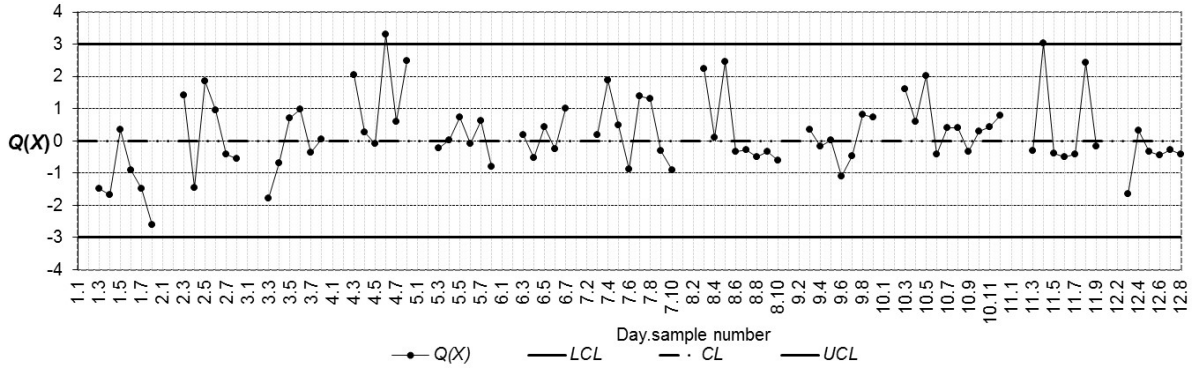

Fig. 2. Q(X) chart for chromium (Cr)

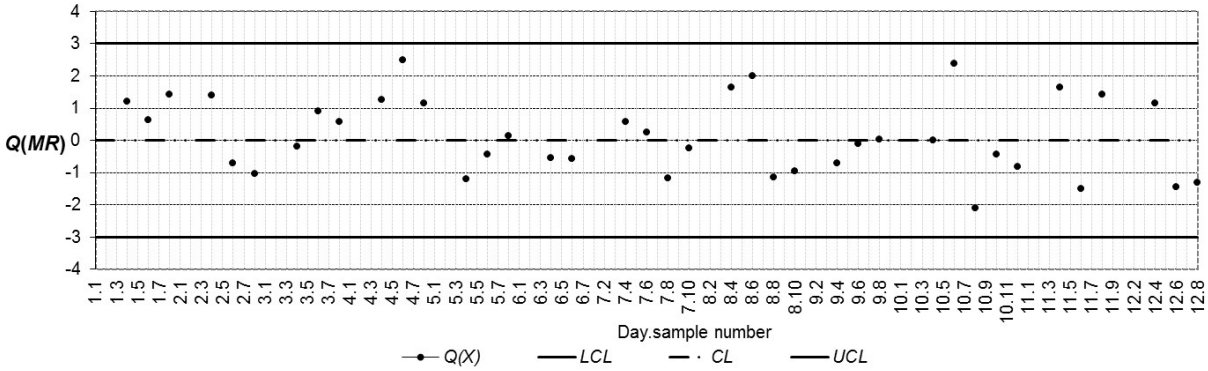

Fig. 3. Q(MR) chart for chromium (Cr)

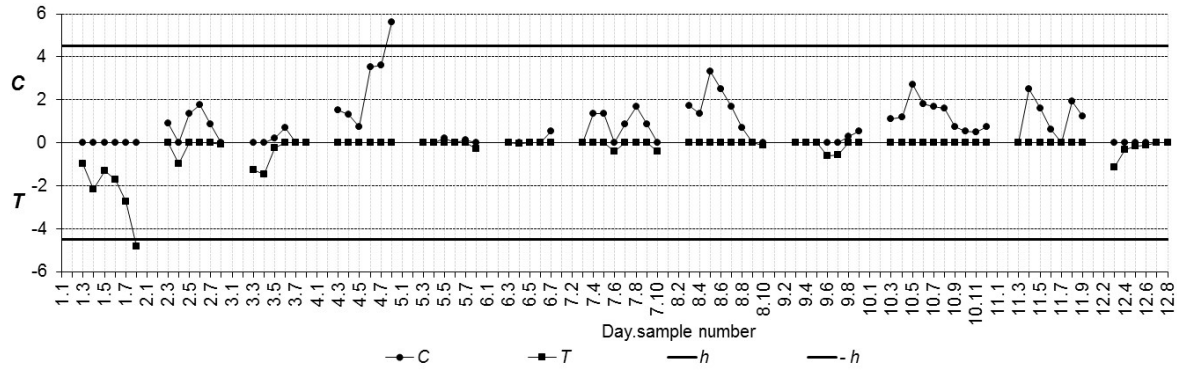

Fig. 4. CUSUM Q(X) chart for chromium (Cr)

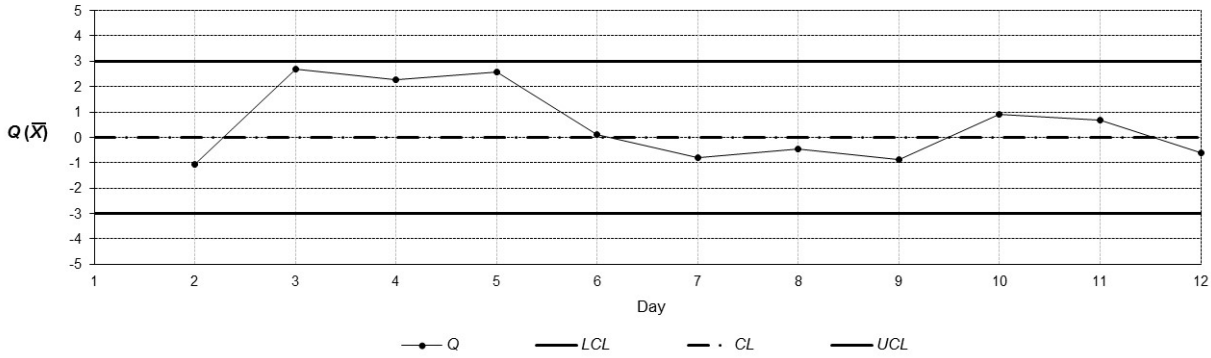

Fig. 5. Q($\bar{X}$) chart for chromium (Cr)

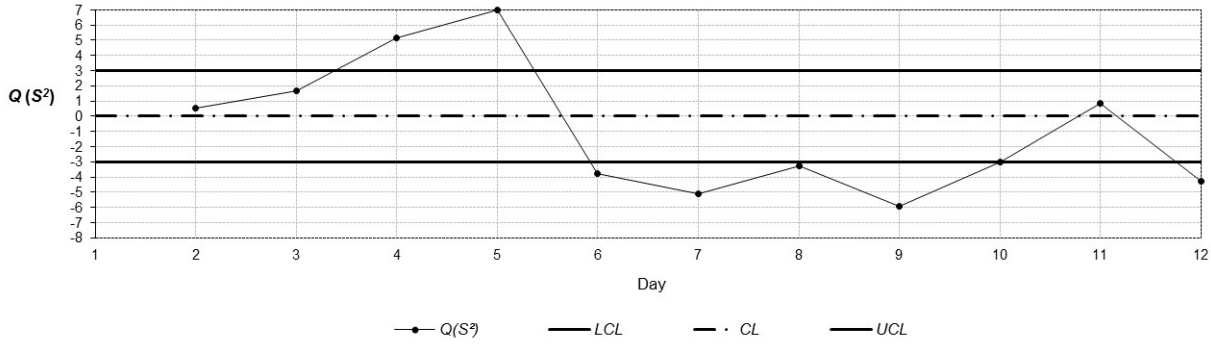

Fig. 6. Q(S^2) chart for chromium (Cr)

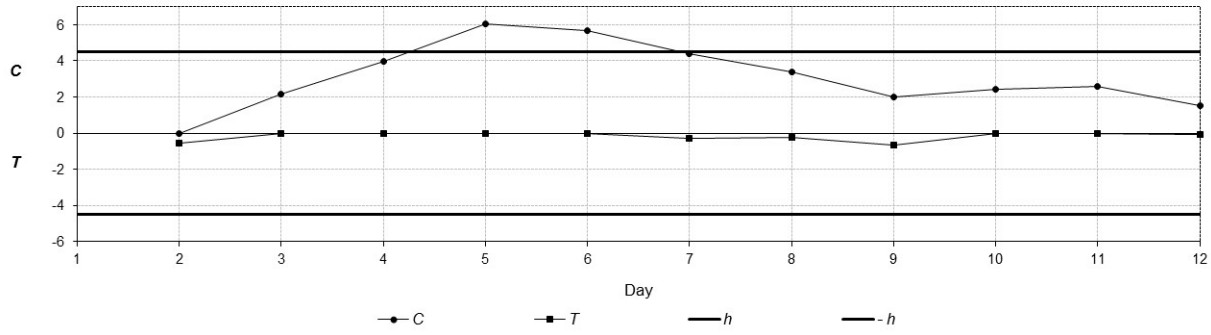

Fig. 7. CUSUM Q($\bar{X}$) charts for chromium (Cr)