

PROCESSES ASSESSMENT AND MONITORING IN A CLINICAL LABORATORY

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1 INTRODUCTION

Nowadays demands for quality continue to grow not only in production, but also in services. Service is an activity which takes place between a customer and a provider. There is a disadvantage compared to a product – service is more difficult to provide and mainly, it is more difficult to set measurable parameters of a service. Quality of health care services is a very sensitive subject, it is important for not only the health care providers. It is very important for state administration, health insurance payers and mainly the public, the potential patients.

There are three dimensions of the healthcare services quality (Madar, 2004):

- Quality of the service from the client's view point;
- Quality of the service from the view point of management – the most economical and most efficient use of resources within the framework of directives and limits, set by superiors or payers;
- Quality of the service from the professional view point – if the services fulfill the needs in the way as they are defined by professionals who execute them or who send patients to take the service and if the services contain suitable techniques and procedures, which are necessary for fulfilment of client's needs.

The article focuses on the services provided by a clinical laboratory from the professional view point. Its performance can be measured only when the performance indicators are correctly set and measured.

The objective of this article is: To set indicators for measuring the ancillary processes capability and to amend the quality indicators in a clinical laboratory with capability indexes as far as processes assessment is concerned, and with control charts with moving limits for analytic phase processes monitoring .

Contribution of the article is expected in following areas:

- Assessment of the analytical phase processes performance;

- Based on the processes performance, setting up of a methodology for usage of the tools to determine frequency of running control samples within the internal quality control;
- Reduction of the laboratory services costs by setting up a suitable frequency of running control samples;
- Assessment of the use of moving control charts for processes monitoring.

2 METHODOLOGY

The services provided by clinical laboratories are unavoidable in the health care system. The results of analytical testing have a strong impact in medical treatment. The results can influence (even fatally) the patient's health, quality of life and sometimes the life itself. The results of tests are the basis for important decisions on diagnosis, prognosis and the way how to proceed with medication. That is why the quality of the tests results is so important (precise and accurate) and the laboratory response time (time from receipt of samples to despatch of results) minimal. Nowadays, when laboratories use fully automated analysers, the response time is not a problem any more. The quality of results is closely connected with assessment of capability of all processes and sub-processes in a laboratory.

The quality level assesment is based on comparison of what really is with the vision what should be the optimum of quality. The result of the assessment therefore has influence on determination of what should be and detection of what really is. In the health care this problem is long time focused on by the Joint Commission on Accreditation of Healthcare Organization (JCAHO) and the national or international standards are considered as the vision of the optimum of quality (Zgodavová, 2006).

In the Czech Republic the capability of clinical laboratories is being assessed according to the standard ČSN EN ISO 15189:2007 – Clinical laboratories – Special demands on capability and quality. This European standard has been approved by CEN and it is used by clinical laboratories to develop their quality management systems and self-assessing of their capability. It is also used by accreditation bodies to assess the clinical laboratories capability.

Clinical laboratories can supply 70% of information about patients, When these information are irrelevant, they cannot help neither the doctor, nor the patient – more to the contrary. How to define quality in a clinical laboratory? The American Institute for Quality (Richardson, 2003) suggested to define the quality in a clinical laboratory as the „Laboratory system for collection, examination and issuing of results of human samles, which :

- Supports diagnosis, prevention and management of ill conditions;
- Gives information of a clinical importance about patient's health status;

- Meets the requirements on accuracy, repeatability and traceability;
- Tries to minimise mistakes;
- Is quick, safe, efficient and is not expensive;
- Is focused on patients satisfaction and continual improvement.

Laboratory examinations should fit to the clinicians needs, laboratories should ensure the confidence of doctors and patients to the examinations results and to guarantee that the costs were spent efficiently. The definition of quality differs according to view point and needs of stakeholders (Westgard, 2008).

The quality of laboratory examinations depends on many factors. Some of them can be influenced by the laboratory management, some originate outside the laboratory, mostly within the pre-analytical phase. Suitable quality indicators can be selected on the basis of three different principles, which represent three different concepts (approaches, models) of quality. The concepts are based on three models: analytical, biological and clinical ones (Hyloft, 1994).

In the laboratory it is possible to identify processes and class them into groups:

- Managing processes – are used to control the laboratory functioning;
- Main process – examination of biological samples, the output of which is determined for laboratory customers;
- Processes of resources management – are used to control resources the laboratory uses;
- Ancillary processes – these processes support the above mentioned groups of processes.

The main process – examination of biological samples – can be divided into three sub-processes: pre-analytical phase, analytical phase and post-analytical phase. For the main process to functionate well it is necessary to ensure that also the ancillary processes are set and function well (Fig. 1).

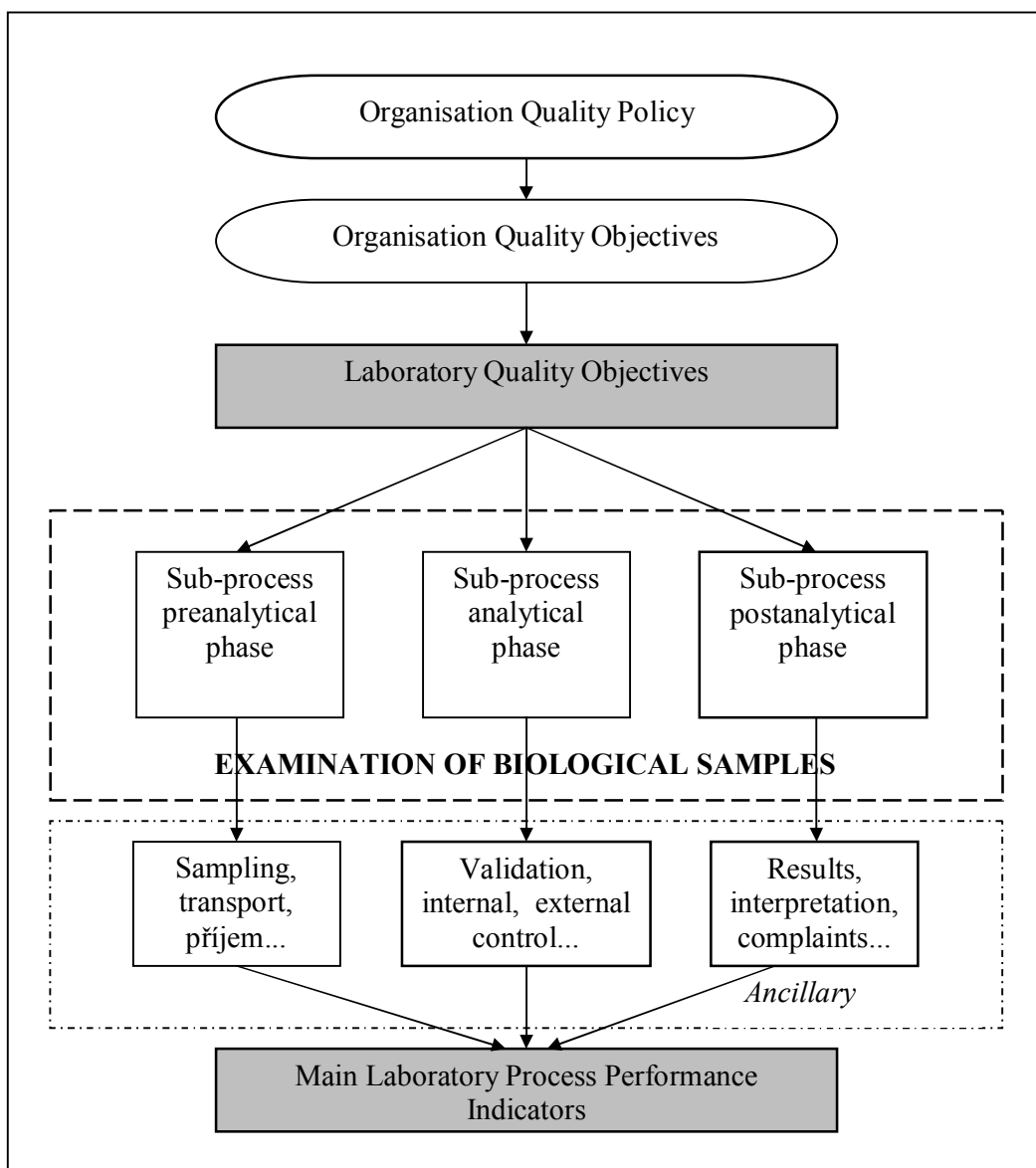


Fig. 1 - Algorithm of processes performance indicators (modified with author permission) (Nenadál, 2001)

Sub-process Analytical phase performance indicators

The performance of the sub-process Analytical phase is measured through assessment and monitoring of examinations performed. After the Internal Quality Control has been mastered, the process performance is measured also by the External Quality Control. Monitoring of the examinations is a logical follow-up

of validation, resp. verification. When the IVD (In-vitro diagnostics) validated by their manufacturer are used, verification only is enough to measure examinations.

Verification

To measure the sub-process „Analytical phase“ by the ancillary process Verification we use following parameters: accuracy, precision, process capability.

Accuracy indicators: SD, CV

Precision indicators: Bias %

Capability indicators: sigma capability, capability indexes

For measuring – monitoring of the ancillary process internal quality control the Control Charts are used.

Parameters: control charts,

Indicator: SD, data mean

For measuring of the ancillary process external quality control we focus on how the laboratory succeeds in the given cycle of controls:

Parameters: success in the given cycle, success in the last 2 years

Indicators: TE, Z – score

Verification of the analytical process contains, according to recommendation of the professional associations, the parameters accuracy and precision. In this article also capability will be included to these parameters and it will be described by capability indexes.

Processes monitoring

For monitoring of the analytical processes laboratories use control charts, which are valuable quality control tools. They are very significant, because when they are rightly chosen and interpreted, they give valuable information about the process (examination procedure, testing of a sample) behaviour and performance. Basically, the control charts should be used as a diagnostic tool to assess if the process tested behaves in the way we expect. Analysis of the control charts can detect in advance significant deviations of the process from the set levels, find and explain the causes and perform corrective actions.

The choice of a control chart depends on character of the measured data and their probability distribution. Then we are able to calculate the control limits. When the control chart is chosen incorrectly, the probability of detection of process deviations decreases. In reality it means that, for example, we can get data points out of control limits even in cases of no change in the process. To be able to fully utilise the advantages of control charts, the data distribution must be Gaussian (normal). This is the requirement also of the Shewhart's i Levy Jenning's control charts, which are mostly used in clinical laboratories (ISO 8225).

When the data distribution is not Gaussian, it is necessary to use an alternative control chart instead of the Shewhart's one, for example the EWMA chart with moving control limits. As shown on Figs 2 and 3 (analyte fT4), when the EWMA is used, the number of rules violation is significantly reduced. The charts have been constructed with the use of real data, analyte fT4 (free-Thyroxine).

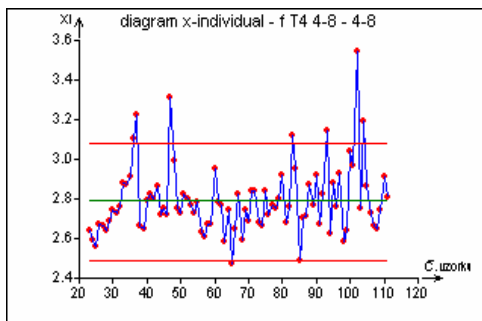


Fig. 2 Shewhart's chart x – individual with dependant data fT4

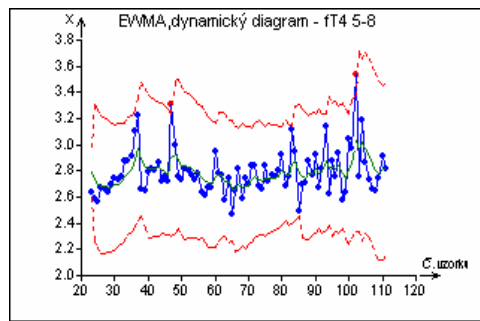


Fig. 3 EWMA chart with moving limits, analyte fT4

Ancillary process Verification – the use of Capability Indexes

Processes capability

Capability of a process is a measure of the process real quality compared to a standard (specification). We assess it after all the systematic effects have been removed, i.e. in the status when the process is under statistic control. When assessing the process capability, we then assess only the variance caused by random effects. When the variance is too high, process cannot have results which would be permanently „within range“. Such process must be examined and after that corrective action(s) must be taken.

As for verification the C_{pk} indexes were used, other indexes are not mentioned in this article. Index C_{pk} takes to account not only the variability of tested quality parameter, but also the real capability of the process to keep within prescribed tolerance limits. Its value then reflects the ratio of distance of the mean of the tested quality parameter from the closer tolerance limit to a half of real data

variability. Index Cpk can be calculated for both one-side and two-sides tolerances.

$$C_{pk} = \min\{C_{pU}; C_{pL}\}, \quad C_{pU} = \frac{USL - \bar{x}}{3SD}, \quad C_{pL} = \frac{\bar{x} - LSL}{3SD} \quad (1, 2, 3)$$

It is possible to say, that analytical processes with Cpk between 1,0 and 1,33 are reliable. Processes with the Cpk value below 1,0 are less reliable and the probability of incorrect result (non-conformity) occurrence is higher. Processes with the Cpk value above 1,33 are well reliable and with the value above 1,67 they are highly reliable with a very low probability of incorrect result (non-conformity) occurrence (Plura, 2001). Example shown on Fig.4.

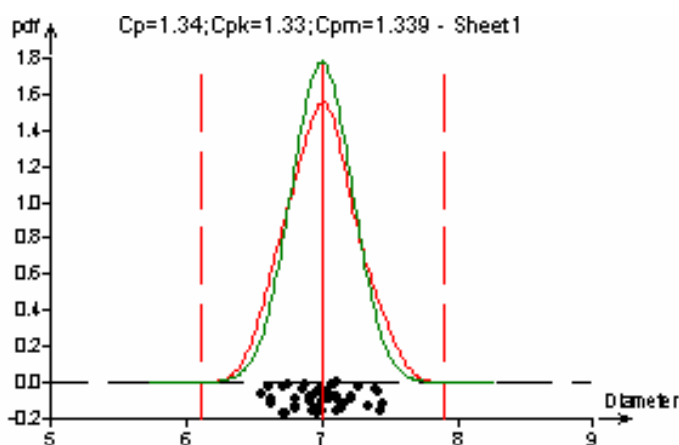


Fig. 4 Probability density curves for $C_{pk} = 1,33$

For verification, which is sufficient for an analytical process assesment, it is nowadays enough to asses accuracy (trueness) and precision, or good results in the External Quality Control. To be able to calculate these indicators, it is necessary to obtain data, which have usually no further use. But, the data could be used for calculation of other processes performance indicators, like, for example, the suggested capability indexes.

The capability indexes provide information about another property of the analytical process. The calculation takes to account tolerable and real process variability, like the Six sigma metrics. The Cpk capability index contains information about accuracy and trueness together. The accuracy is described by means of the standard deviation SD or the coefficient of variability CV% and gives information on accuracy achieved only, but without assessment, if it is still acceptable or not. But the required accuracy of analytes in the biological samples differs according to the biological variability. If the required accuracy is added to the capability criterion, for example $\min. C_p \geq 1,3$, the capability index value returns clear information about acceptability of the variability.

3 APPLICATION

The application part of this work contains evaluation of the use of capability indexes, which were incorporated into verification parameters. The capability indexes were calculated and evaluated for 98 tests at two or three levels. It was found out that 41,06% of all the 263 tests have not reached required capability. Such a high number of incapable tests was caused by including of immunochemical methods of testing. These methods have usually higher variability than other tests (analyzers Architect, Unicel a Stratec). When the capability indexes were assessed without these methods, the number of incapable processes was significantly reduced, down to 27,51%. A very good capability ($Cpk \geq 1,33$) was achieved at 40,1% of all tests, respectively 53,44% without the immunochemical methods. The worst results were noted at the low levels of the analytes, the best results at the high levels.

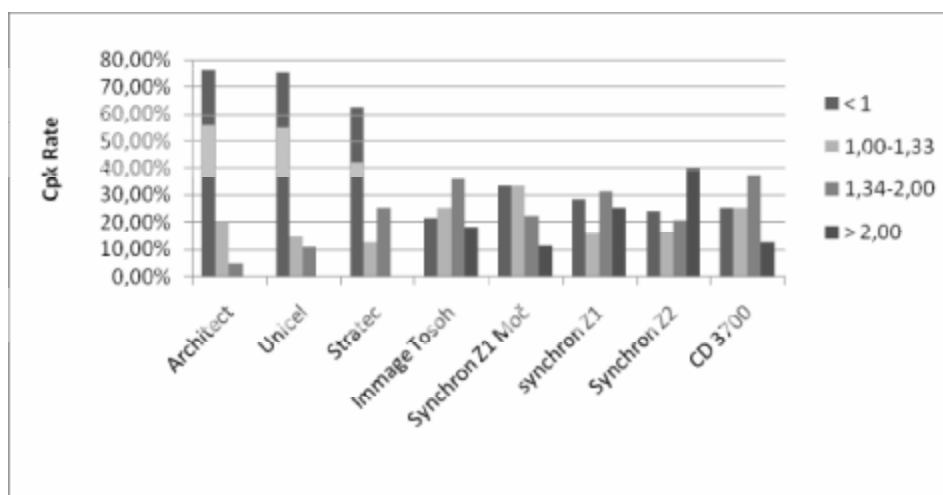


Fig. 5 - The Cpk values rate per analyzer

Further on the analyzers have been assessed independently. As we can see at Figs. 5 and 6, there is a significant difference between immunochemical methods and the other principles. As far as all other principles than the immunochemical methods are concerned, the differences among them are minor. For the Synchron Z 1 a Z 2 analyzers, where tests are performed the same way, there is a difference visible on Fig. 5 in the number of tests with $Cpk \geq 2,0$. This difference is caused by different age of the analyzers. The analyzer Synchron Z 2 has been in use for significantly shorter time than the Synchron Z 1. It means, that capability of analytical processes is indispensably influenced also by the age of equipment.

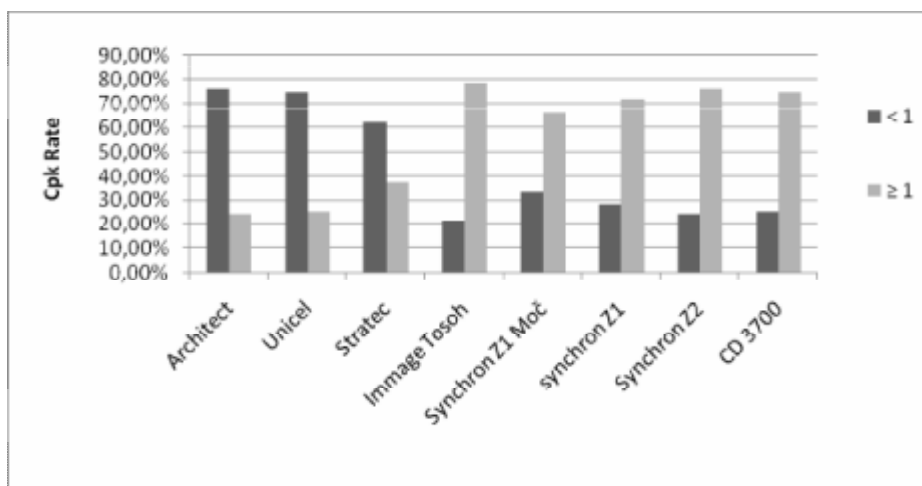


Fig. 6 - The rate of Cpk < 1 and ≥ 1 per analyzer

The Cpk value depends a lot on the required variability. The tolerance range was set according to the recommendation of SEKK (www.sekk.cz). In some cases (for example ALT) it would be wise to adapt the tolerances to concentration levels. If the required test variability is set correctly, it is possible to use the capability indexes for determination of frequency of the control tests performance, as recommended in the Table 1.

Tab. 1 – Capability indexes and frequency of control tests

C_{pk} Value	Capability	Control testing frequency
> 1,0	low	In each series (for example of 20 samples), if the level ifs physiologically important
1,01 – 1,32	acceptable	2 x in each series (for example at the beginning and at the end). Series up to 1 day.
1,33 – 1,67	very good	1 x in each series (serie 1 day)
> 1,67	high	each 2 to 3 series (series 1 day)

Frequencies, shown in the table, are valid for particular levels of concentration of the control sets. In the 1 day series minimally one level must be measured. Correct application of the capability indexes into the clinical laboratories operation can bring significant quality improvement and also reduction of costs, connected with possible reduction of running control tests.

The ancillary process Internal Quality Control – monitoring by classical EWMA chart and EWMA chart with moving limits.

In the last few years we can see comments in professional literature and also coming from laboratories calling attention to frequent cases of automated processes, where regulation by the classical control charts (Shewhart's type) is inadequate or impossible. These charts were introduced at the break of the twenties and the thirties of the last century and were intended for controlling measurable and attributive parameters (Michálek 2003, Montgomery 2001, Zvárová 2002).

Classical SPC methods, developed for the conditions prevailing in production, perform well only if following criteria are met:

- The details about process are obtained in regular intervals by collection of data in selections of the range $n > 1$
- Collected data are statistically independent within the selection and among themselves
- The selections are made the way to form logical sub-groups (it must be ensured that among the elements of the selection there are no determinable causes of variability)
- Data come from identical statistical distribution (for continuous stochastic variables we usually expect Gaussian – normal distribution).

When these assumptions are not adhered to, the classical SPC methods fail. The SPC system in this case more frequently than it was estimated falsely signals that there are determinable causes influencing the process and therefore that the process is not under statistic control (Noskievičová 2003; Michálek 2003).

EWMA Charts

EWMA charts were introduced in 1959. It is abbreviation of Exponentially Weighted Moving Average (sometimes called exponential forgetting). Its use is similar to Shewhart's charts. With advantage it is used in cases when we cannot guarantee conditions necessary for use of the Shewhart's charts (normal distribution, independent data).

In situations, when data are dependant, it is possible to use a modification of the EWMA chart – the EWMA with moving limits, a chart with one step prediction of mean and variability.

The EWMA chart with moving limits is suitable for processes, where the parameters show possitive autocorrelation and the proces has a non-constant mean which changes slowly.

Interpretation of the EWMA chart with moving limits is identical to interpretation of other control charts. If all the values of measured parameter x_k are within the control limits, the process is considered under statistic control and changes in the process are slow. If some of measured values lies outside the control limits, it should be considered a signal that the process is out of statistic control (Tošenovský, 2000).

On Figs. 7 and 8 there is an example shown where for the same dependant data the classical EWMA chart and EWMA chart with moving limits are used. The classical chart requires higher necessity of intervention to the process, which proves the false signal. Also the quickness of detection is different (Kupka, 2001).

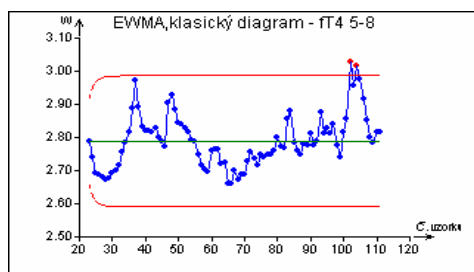


Fig. 7 Classical EWMA Chart, analyte ft4

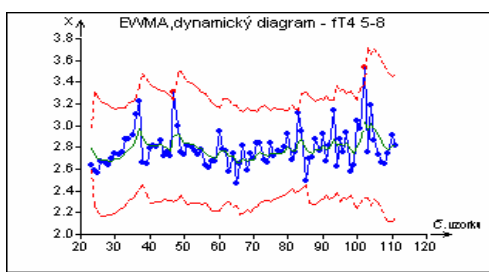


Fig.8 – EWMA Chart with moving limits, ft4

To compare the Shewhart's control charts X-individual + R and the EWMA charts several representatives of clinical examinations were chosen on the basis of the explorative analysis. The data have been processed by means of statistical software QC-Expert. Creation of the Shewhart's regulation charts depend on data Gaussian distribution and data independency. The explorative analysis found several variants of the requirements violation. In some cases the data had Gaussian distribution and were independent, which is the requirement for Shewhart's charts creation, in some cases the data did not have Gaussian distribution but were independent. The last case was that the data did not have Gaussian distribution and were dependant. Each of the mentioned variants has been processed. Further on the examinations were chosen, for which both of the chart types were created. The examinations were chosen taking in mind that they should cover most of the analytes, according to their structure and function (enzymes, sacharides, lipides, proteins, ions, tumor markers a hormones).

For 29 compared analytes the Shewhart's charts, classical EWMA charts and EWMA charts with moving limits were created. With the total number of 4605 data, the numbers of data outside limits for Shewhart's and classical EWMA charts do not differ significantly (229, resp. 239); the classical EWMA chart refused more data only by 4,4%. There is a significant difference between those

two charts and the EWMA chart with moving limits. When it was used, the number of refused values is only 53, i.e. 4,4 times less.

4 CONCLUSION

Analytical processes assessment

Within the frame of verification, which is enough to assess the analytical processes, nowadays only accuracy, resp. trueness are evaluated, eventually also the success in the External Quality Control. To be able to assess the parameters we need to measure data which are not used further more. The same data can be used for calculation of other process performance indicators, like the suggested capability indexes, namely the Cpk, which contains both the information about accuracy and precision. If the required accuracy is included into the capability criterion, for example $C_p \geq 1,3$, the capability index can give a clear information that the variability is acceptable or not. Using the Cpk capability index we get information how the process performs against the required target value, i.e. about the process trueness, which is normally described by bias%. Incorporation of the capability indexes to the parameters of validation/verification would mean that more information about analytical processes could be obtained.

Verification of analytical processes was extended by the use of capability indexes. 98 different examinations have been assessed, each at min. two levels. The assessment of analytical processes by means of capability indexes can be used for determination of control samples testing frequency. Correct monitoring of the processes is very important for the quality of the examinations results, which are used for treatment of both ill and healthy patients.

Monitoring of the analytical processes

The assessment of EWMA charts usability for monitoring of processes was performed at different combinations of data properties. When the conditions for Shewhart's charts were met (i.e. independent data with Gaussian distribution), the classical EWMA chart was more sensitive to a systematic error. In case of dependent data, we can estimate that signal given by this chart is false, idle, because the chart with moving limits does not detect the limit violation. The variation was small, it is so unimportant and the process remains in the stable status. In the two cases data measured within one month were used. In the third case for the charts creation data measured within six months were used. The difference between various charts is higher in this particular case. While Shewhart's x-individual and classical EWMA charts signal more frequent violation of the limits, the EWMA chart with moving limits signals the same only once.

Further it was discovered and compared, that data coming from the same process, but on different concentration levels of the measured analyte, have in the same time period different character. For this assessment data from one month

only were used, but tested twice a day, which meant doubled number of data compared to previous months. The higher the number of data was, the higher was the difference among usage of various control charts. The reason was that data change their character in time.

The performed analyses lead to conclusion that the usage of EWMA charts in clinical laboratories is possible, but it is not necessary for monitoring of the processes. In laboratories the values are recoded to the control charts once or twice a day, only rarely more frequently. The time period, which is important for an analyst, is maximally one month. With this volume of data there was found no significant difference among the compared control charts. The false signal about the limits violation comes out in a longer time period (4-6 months), but it is worthless information for the laboratory operation. The usage of EWMA charts, namely the chart with moving limits, is suitable for processes, where the test measuring is performed more frequently, apparently at production processes.

The alert to the incorrect use of the Shewhart's control charts due to inappropriate data properties has not been confirmed in a clinical laboratory operation. The false signal moreover occurs only in case when no deviation happened. The case, when all the points would be falsely within the control limits, has not occurred. This means that any intervention to the process would be needless, not that the violation would not be detected. The number of false signals in a clinical laboratory is minimal, therefore also the needless interventions costs are minimal.

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