Point-of-Care Testing **Edited by: P.B. Luppa**

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The extended internal QC (eIQC): a new practical approach for quality assurance in point-of-care glucose testing using the POCTopus Software – a pilot study

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Abstract

Background: Quality assurance (QA) in point-of-care testing (POCT) is an important issue for organizing POCT structures within the healthcare sector. In Germany, only one device needs to participate in an external QA program, if the responsible core laboratory is supervising internal quality controls of all other identical POCT devices. This flexible definition of quality control (QC) testing is in line with the fundamentals of ISO 22870 and the ISO 15189, but can only be regarded as a minimum requirement.

Methods: We present a pilot study for an inexpensive new approach for additional POCT QC measurement similar to the external QA program within the medical laboratory using capillary glucose measurement as an example. This new system, referred to as "extended internal QC (eIQC)", uses in-house generated QC material from leftover full blood from routine diagnostics. We provide information on calculation of target values and acceptance ranges and preliminary data on stability and comparison between POCT and core laboratory testing (COBAS 8000). Additionally, we simulated the approach using three devices within the laboratory as surrogate for three POCT sites. In this pilot study, measurements of QC material beyond the mandatory QA plan are structured and optimized through the use of the POCTopus Software solution.

Results: QC material was easily generated including specification of target values. The software aided in automatized processing of the samples. The software showed limitations in evaluation and monitoring without relevant use of resources. We found a significant bias between measurements on POCT and COBAS 8000 instruments.

Conclusions: The presented new approach for additional QAs for POCT enables POCT coordinators to establish an additional safety and QC level. Further software improvements are required. Further studies are needed for validation and comparison measurements between methods. Overall, this approach offers great potential for POCT structures seeking higher quality standards.

Keywords: internal quality control; POCT; point-of-care testing; quality assurance; quality control scheme; software.

Introduction

Quality assurance (QA) for all medical laboratory testing is an important issue for organizing valuable analytical structures within the healthcare sector. Fundamentally, laboratory test results are subject to the same reliability criteria whether they are generated in the core laboratory or as point-of-care testing (POCT). Besides other factors, the number and frequency of tested internal and external quality controls (QC) defines the level of adequate quality [1]. Therefore, a robust QA scheme is necessary to deliver high-quality laboratory testing. As this applies also to any kind of POCT, supervision thereof is crucial. However, QA programs of laboratories are nowadays more often defined by risk assessment and are focused more on the probability of harming a patient compared to identifying and monitoring wrong QC results of preceding days [2].

The International Organization for Standardization (ISO) standards ISO 22870 and ISO 15189 allow a flexible definition for a POCT QA plan [3]. Every laboratory is obliged to set up an appropriate plan for routine QC measurements. POCT organization should inherit a POCT committee, a POCT coordinator for the entire hospital as well as one for each unit providing POCT and educated POCT users [4].

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In Germany, the "Guideline of the German Medical Association on Quality Assurance in Medical Laboratory Examinations" (Rili-BÄK) regulates the internal and external QA plans more rigidly, depending on the technical device used for testing [5]. The results must be evaluated according to the Rili-BÄK table B1 column 3, defining the allowed deviation in internal QC. For devices with an integrated electronic system check and unit-use reagents, only one internal QC per week is mandatory. Additional controls, however, are required after calibration by the user, after repair or maintenance work or when reagent batches change.

In cases of unit-use devices without an electronic physical standard or in more complex POCT devices with built-in reagent supply, such as blood gas analyzers, the internal QA plan is similar to laboratory tests performed on high-throughput devices: At least two QCs in different concentration levels have to be measured every day on each device. However, only one participating device, substituting for all identical devices within one healthcare setting, performing the quarterly external QC is required to adhere to the German Rili-BÄK guideline. The mandatory condition is that the medical laboratory is responsible for supervising the internal QC of all POCT devices within its organizational unit, e.g. a hospital. General practitioners are exempted from mandatory external QC measurements.

The described Rili-BÄK rules can only be regarded as minimum requirements and are embedded in an overall quality management system (QMS). POCT should be governed by a POCT committee, a team of core laboratory experts, being responsible for the POCT QMS, and a POCT coordinator. The coordinator organizes all POCT processes in terms of specifications for the preanalytical phase, for the individual tests, for the post-analytical phase, for staff training, as well as tasks and responsibilities for conducting the appropriate QC strategy. The discussions on how mandatory QA plans should be defined are therefore lively. Some individual medical laboratories in clinical units with high volumes of POCT measurements extend the number of QC measurements beyond the Rili-BÄK or ISO specifications. For example, additional testing of external QC samples at different POCT sites within one hospital enables a comparison of various devices in relation to the single instrument used for the EQA measurements.

In this pilot study, we propose a practical and inexpensive approach for additional internal QC for POCT, using capillary glucose measurements as an example. We aimed to provide the basic ideas of this approach for further discussion including results of corresponding experiments. This new system could fit in a standard hospital POCT environment and takes limited human resources in the medical laboratory and on the wards into account. This proposed system, referred to as "extended internal QC (eIQC)", is embedded in a POCT middleware, which provides sufficient process control and meaningful evaluation.

Materials and methods

Improving a QA plan based on additional measurements is the basis of this new eIQC approach. Based on the example of POCT glucose measurements, the creation of these additional QC samples and their usage are presented below, categorized in separate process steps. As software aiding to manage and evaluate the QC measurements, the POCT Software POCTopus (OSM, Berlin, Germany) was used in this pilot study.

Sample preparation

Some frameworks (Rili-BÄK) suggest using QC sample matrices as similar as possible to patient samples. Most POCT QC sample matrices are water based and not comparable to human blood or serum. Therefore, the full blood QC samples evaluated in this investigation are pooled from sodium-fluoride (NaF)-blood anti-coagulated leftover blood of clinical routine diagnostics. In order to produce two QC pools with target values as close as possible to the desired concentration, leftover blood samples from patients with known plasma glucose values, corresponding with these targets, were collected. Due to the fact that these leftover blood specimens were pooled and not used as single patient samples, there was no need for a vote from the local Ethics Committee. The target values were selected to reflect a physiologic blood concentration (60–100 mg/dL) as well as pathologic glucose concentrations (under 50 mg/dL or above 130 mg/dL). The glucose concentrations of these two pools were measured with two different NOVA StatStrip devices (NOVA Biomedical, Waltham, MA, USA) in the medical laboratory 3 times and the average of these six measurements was calculated. If all results were within a 10% range from this average, this pool was accepted as QC material. The acceptance range for preparation should strictly be adhered to in order to exclude unknown matrix effects, potentially influencing the measurement. Hence, if any measurements should deviate beyond the analytical range of target values, the whole pool must be discarded.

The calculated average value of the six measurements was defined as target value for this QC level. The acceptable bias from the QC target for the glucose eIQC was set at ±15%, according to the external QC requirements of the German Rili-BÄK for blood glucose (column 5 of table B1) [5].

For every participating POCT site, two capillaries (140 µL, Multi Cap-S, Siemens Healthcare Diagnostics Inc., Erlangen, Germany) were prepared, containing one QC level each. The capillaries were filled and sealed with capillary ends (Capillary Caps for Multi-Cap, Siemens Healthcare Diagnostics Inc., Erlangen, Germany) and labeled with sample information generated by the used software.

For a preliminary evaluation of the stability of these samples, one lot was additionally stored at 4 °C and tested 24 and 48 h after preparation.

Additionally, a comparison between a laboratory method and the POCT method was performed. Triplicate measurements of the QC pools on clinical chemistry analyzers (COBAS 8000, c701, Roche Diagnostics, Basel, Switzerland) using a special method for hemolyzed full blood were analyzed and compared to the results of the POCT devices. The average and deviation between these results and the ones measured on POCT devices were calculated.

Software measurement

In this investigation, we used the POCT administration software "POCTopus" (OSM, Berlin, Germany). New QC samples are created by generating a sample number, inserting the new target values and the allowed deviation. The software creates corresponding barcodes including information on the QC sample numbers as well as the date of expiration. Target values as well as the acceptance ranges are transferred into the middleware.

Alternatively, a paper-based documentation may be chosen. In this case, samples are handled as patient samples. An "eIQC-Patient" is created for each QC level. Ultimately, the results are transferred in accordance with the local laboratory setting.

Distribution of QC samples and measurements on POCT sites

After sample preparation, labeling and software setup, the QC samples should be distributed to the participating POCT sites. The measurements are done on the same day by regular staff doing patient sample measurements and regular internal QC. After barcode scan and measurement, results should be sent to the central POCT software server.

For this investigation, a simulated approach was chosen. Three different POCT devices located in the medical laboratory were chosen to simulate three different POCT sites. The prepared capillaries were tested on these three devices by a different user than the one preparing the samples.

Evaluation

After measurement and result transfer, an evaluation was performed. In case of deranged QC results, the laboratory contacted the responsible POCT coordinator, organizing follow-up corrective actions.

Results

As this investigation only aimed to prove a simulated concept, results of a limited example from February 2020 are presented. The results of the setup measurement including the acceptance ranges of this example are shown in Table 1 for two levels. Both levels were accepted while all single results were within the acceptance range

Table 1: Example of a setup measurement and calculation of target values and acceptance ranges for an eIQC on two POCT devices (StatStrip 1 and StatStrip 2).

	Level 1		Level 2	
	StatStrip 1, mg/dL	StatStrip 2, mg/dL	StatStrip 1, mg/dL	StatStrip 2, mg/dL
1. Measurement	79	77	138	144
2. Measurement	82	77	138	145
3. Measurement	78	75	147	140
Average (target value)		78		142
Acceptance range preparation (±10%)	70	86	128	156
Acceptance range for eIQC (±15%)	66	90	121	149

from 70 to 86 mg/dL for level 1 and from 128 to 156 mg/dL for level 2. The range for acceptance of the eIQC results of POCT sites was calculated as 66–90 mg/dL for level 1 and 121–149 mg/dL for level 2.

The results of the comparison between StatStrip devices and COBAS 8000/701 show relevant deviations of more than 10% between blood glucose levels measured from full blood NaF samples (Table 2). The average for both instruments showed a 22% lower result for StatStrip in comparison to COBAS for level 1 and a 13% lower result for level 2.

Stability measurements after 24 h and 48 h of storage at 4 °C for two sample lots are shown in Table 3. The decrease within 24 h was just 1–2% for both levels in both lots. Within 48 h a greater heterogeneity of stability was discovered between the two lots (1–13%).

Three simulated POCT sites participated in this QA scheme. The results and interpretations of their measurements are shown in Table 4. The deviation from the target value was very limited (–3% –5%) for all sites. All simulated sites passed the eIQC.

Discussion

The measurement of blood glucose is relevant in diagnosing and monitoring diabetes. The quality of determination the blood glucose heavily influences the clinical quality of diagnosing and treating these patients [6]. POCT devices are more often affected by deranged QC results in external QA programs than measurements from analyzers within medical laboratories [7]. Due to the high impact of glucose determination in clinical settings and the known problems, it is important to maintain high quality in assessment of blood glucose measurements in POCT settings.

Additional measurement of QC material similar to the external QA program within the core laboratory is currently already being implemented in some selected

Table 2: Results of POCT devices (StatStrip) in comparison to clinical chemistry analyzer (COBAS 8000/c701).

	Level 1			Level 2		
	StatStrip, mg/dL	COBAS, mg/dL	Deviation	StatStrip, mg/dL	COBAS, mg/dL	Deviation
1. Measurement	72	95		126	146	
2. Measurement	75	97		136	146	
3. Measurement	76	94		121	149	
Average	74	96	–22%	128	147	–13%

Table 3: Stability of blood glucose concentration in capillaries with sodium fluoride stored at 4 °C.

	Lot 1		Lot 2	
	Level 1, mg/dL	Level 2, mg/dL	Level 1, mg/dL	Level 2, mg/dL
0 h				
1. Measurement	79	138	68	132
2. Measurement	82	138	64	136
3. Measurement	78	147	64	134
Average	80	141	65	134
24 h				
1. Measurement	78	144	65	128
2. Measurement	80	138	62	132
3. Measurement	78	135	65	133
Average	79	139	64	131
Deviation	–1%	–1%	–2%	–2%
48 h				
1. Measurement	77	119	64	134
2. Measurement	81	110	66	137
3. Measurement	78	140	65	139
Average	79	123	65	137
Deviation	–1%	–13%	–1%	2%

Table 4: Results of the simulated eIQC test on three different POCT sites.

	Level 1, mg/dL	Deviation level 1	Level 2, mg/dL	Deviation level 2	Passed
POCT site 1	79	1%	138	−3%	Yes
POCT site 2	82	5%	145	2%	Yes
POCT site 3	78	0%	148	4%	Yes
Target range	66–90		121–149		

hospitals. The use of additional QC measurements improves the test quality even though it is currently not mandatory. Different approaches show that the number of different QC materials and the frequency of measuring QC directly influence the quality of analytical testing and subsequently patient safety [8]. Predefined QA plans by, for example, regulatory bodies could hardly define an acceptable risk for harming patients in all healthcare settings. A customization of QA plans is therefore necessary based on a profound local risk assessment [9].

Structuring these additional measurements usually requires both significant staff and financial resources. QC measurements beyond the mandatory weekly testing could be structured and optimized through the use of advanced software solutions. The used software needs to support the processing and evaluation of the new internal QA program with an intra- and inter-hospital QC trend analyses and benchmarking.

Our results show that setting up such a QA approach is possible with limited staff resources. Due to relevant deviations between the POCT testing technique and wet chemistry technique used on high-throughput devices in medical laboratories, the measurements for calculation of target values need to be done on devices identical to those off site. As other studies do not show significant differences between POCT and laboratory glucose measurements, matrix effects, methodical differences or even preanalytical factors must be discussed and further bigger studies are needed for clarification [10–14]. In routine practice, also handling errors must be considered [15]. According to the results of our stability experiment, the in-house prepared QC samples may be stored up to 24 h at 4 °C. Hence, preparation of QC samples can be done 1 day prior to distribution to offsite POCT facilities, which could be relevant for larger POCT settings.

The tested software "POCTopus" we used for organizing eIQC is easy to use. It requires only target values with an allowed deviation, the number of needed samples and the frequency of QC measurements. As we could show, the calculation of target values is based on replicate measurements on devices identical to the ones the QC will get measured on. The allowed deviations/acceptance criteria may be adopted from the Rili-BÄK and the frequency of measurements has to be defined by the POCT coordinator based on the analytical throughput of each device.

Many steps like an optimized evaluation of the eIQC results or creating QC certificates are currently not implemented in the middleware and still leads to consumption of human resources. Organization, monitoring and evaluation of the results should be completely automated. Certificates should be generated by the system and sent to the participating unit electronically. The eIQC program could provide a status report of all units including their available QC results, making surveillance of all POCT easy, including information on QA participation and pass rates.

Concerning the QC sample materials, there are still many issues to be addressed yet:

1. Manufacturer of POCT devices should be aware of the necessity to create in-house prepared QC materials and therefore extend the authorized materials for their tests in this context.
2. For the usage of patient blood samples, there are legal aspects to be clarified. Under certain circumstances, the patients' informed consent has to be obtained.
3. Hygiene aspects must be considered. All users should be aware that these QC samples are potentially infectious materials.

As a limitation of this proposal and pilot study, several issues need to be considered. The power of this study is limited due to its low number of samples. For routine implementation, further validation and stability studies, using samples with a wider range of tested glucose concentrations, are necessary, including matrix effects and linearity. Additionally, a final validation and approval of the used software is recommended.

This proof-of-concept investigation demonstrates the potential of an eIQC approach for the blood glucose POCT setting. For implementation of this approach, the presented software solution offers the ability to set up this additional QAs of POCT capillary glucose measurement and enables POCT coordinators to establish an additional safety and QC levels. In order to implement this approach in a routine setting, further validation and stability studies are needed and the evaluated software should be extended by some additional features. The presented approach

offers great potential for POCT structures seeking higher quality standards.

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