Appendix A

Quality Assurance (QA) in Clinical Laboratory (1,2)

Introduction

Starting from the assumption that each laboratory result is affected by different types of errors (systematic and random errors), it is imperative to prevent errors that can occur everywhere during the process between the clinician requesting a clinical biochemistry test and the result of the test.

The entire process can be performed in the lab or in the clinic for the point of care testing (POCT).

Each of the 3 ST phases is characterized by the following procedures:

Pre-analytical phase: manage the requisition form, prepare the patient (including information and/or sign the informed consent), collect the sample, identification of samples, storage, transport

Analytical phase: calibration, quality control procedures, pre-treatment of samples, analyte/s measurement, maintenance of the analytical system

Post-analytical phase: test report

The Quality Assurance in Clinical Laboratory ensures that the results issued do aid in the provision of optimum patient care. It consists in control strategies as standard operating procedures (SOP) and control tools aimed to reduce errors. Many laboratories participate in accreditation programs that stimulate further quality improvements.

Quality Assurance for Sweat Testing

Despite the technological upgrade, the sweat test (ST), validated in 1959, is still operator-dependent. Due to the importance of a pathological value it should be performed as recommended in international guidelines.

Quality control strategies in the pre-analytical phase (see also **Table 1**)

The pre-analytical phase of the ST includes several steps from the patient's information, subject's suitability, sweat stimulation and collection. Each step equally contributes to the final goal that consists in the sufficient weight or volume of sweat obtained. This phase is crucial both as it is at the beginning of the entire examination process and as it is operator-dependent. An adequate sweat sample can be challenging in infants who often result in failed sweat collection reported as the Quantity Not Sufficient (QNS). Currently the QNS is a single quality indicator of the ST pre-analytical phase. It does not take a part of the external quality assessment (see below). The laboratory should keep a record of the QNS rate and review it on a regular basis (**Table 1**). An important quality indicator is the QNS rate: it consists in the percentage of sweat tests without an adequate sweat sample weight/volume. If the QNS rate is unacceptable (**Table 1**), every single step in the pre-analytical phase needs to be audited. It includes a retraining of personnel on: patient conditions, pilocarpine solutions, filter or gauze pads, iontophoresis current source and electrodes, fixing electrodes and collection material on the skin, sweat stimulation and collection time.(3) To improve the QNS rate carefully follow the procedure in **Table 1**. A useful quality assurance strategy is also consistent in bilateral testing: it is a further indicator of a good performance in the pre-

analytical phase of sweat testing as the sweat chloride from two sites should fall within 10 mmol/L for values ≤60 mmol/L and within 15mmol/L for values >60 mmol/L.(4)

Quality Control tools in the analytical phase (**Table 3**)

- Internal Quality Control (IQC) is performed within a laboratory to measure the precision of test results. Control materials (usually liquid controls) are used to monitor the test system and validate patient's test results. A control sample is a stabilized liquid matrix with a predetermined range of result values that simulates a patient sample; this range of result values are not blinded to the laboratory. Control samples are tested in the same way as patient samples and applied in each sample batch run. If the control sample results are not within the acceptable ranges, a problem in the test procedure, equipment or samples themselves should be ruled out. Subsequently the sample batch run cannot be validated as such. There are many criteria and tools for rejecting a test based on the control samples measurements. The Levey-Jennings chart is a simple quality control tool that consists in a graph of the control values to assure that the performance of the analytic system has not been changed during time. (5-7) The Westgard rules are applied to detect true errors and minimize false rejections in a sample batch run to see whether the results from the samples when the control was done can be released, or if they need to be rerun. (8) Patient's results should never be reported until the cause of the problem has been removed. Control materials are retested to check if the problem is definitively resolved. In Europe there are at least 3 commercially available IQC samples. IQC sweat control materials can also be prepared in house as pharmaceutical grade formulations (9)
- External Quality Assessment (EQA) Schemes (10) are performed among different laboratories in the same country or even in different countries. Public or private organizations promote these activities. Each laboratory receives a fixed number of control samples (it depends on the scheme: typically from 3 to 12/round) even accompanied by mock clinical indications. EQA schemes are aimed to evaluate the accuracy (lack of bias) of test results, comparing results provided on the same sample by participating laboratories. Control sample values are blinded to the laboratory. Each laboratory should process the control sample in a fixed time window and communicate centrally the result of the test. Assessment usually covers quantitative analytical performance, but also may include qualitative description of the laboratory, clinical sensitivity (consistency of a sweat chloride or conductivity result with a normal, borderline or pathological range) and the quality of the report. Assessment criteria are fixed by the organization and should be accepted by the

laboratory. Usually at the end of each round, or even after each run, the laboratory receives a final report with a score and recommendations to improve the performance of the test. In Europe there are at least 6 EQA public schemes available.

- Inter-laboratory Comparison schemes are aimed to monitor laboratory performance for accreditation purposes in certain defined circumstances. A reason to use this may be financial or rarity of disease, where no EQA schemes are available.

Quality Control in the post-analytical phase (**Table 1**)

A written report should be provided to the patient for each examination, even if the sample is not adequate (QNS). The sweat test report should fulfill minimum requirements (see **Table 4**). The results should be always interpreted by a consultant (or equivalent) clinical chemist and, if available, also by a CF specialist. The interpretation of test results should be easy to understand.

References

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