Independent quality control and its importance.

# Are you dependent?

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*The ISO 15189 standard recommends the use of independent quality controls. The IVDR also sets out new standards in relation to independent control material. Reagent, instrument, calibrators and quality control material from the same manufacturer represent a closed system, so that in Germany only the Proficiency Test stands as an independent assessment. Is this really enough? Based on a real laboratory situation and three examples from the literature, this article points to the urgent need to use independent control material.*

Keywords: quality assurance, RiliBÄK, reagent lot, lot changes

**The case**

Imagine the following scenario in the laboratory: the telephone rings and you pick up the phone. The clinician or submitter tells you that he has the impression that the sodium levels have been reading higher for about a week. What steps will you take now to handle the complaint?

Typically, quality control data is used to assess the performance of your analytical system. A look at the data shows you that the controls used do not show any abnormalities - your device system is within the limits allowed by the RiliBÄK.

**What now?**

You can look at the sodium levels for all patients in the last week. For example, a daily mean or better median value of patient results can be calculated and, in fact, find that the values are higher overall than in the previous month.

**What happened?**

You have received a new reagent lot and have used it on your analyzer system. Of course you measured the new reagent lot with a new calibration followed by quality control (two controls, one in the clinical decision area, the other in a higher concentration range). The controls showed no deviation from the stated target values and were within the permissible limits of the RiliBÄK.

**Background**

After the production of a new reagent lot, the quality is tested by the manufacturer. One checks whether the performance of the new reagent lot meets the requirements and, if so, the final approved lot is made available for sale. Subsequently, the device system, the new reagent lot, the associated calibrator and the quality control material are used together. This means that a corresponding target value must be determined for the control material. This target value then depends on the device system, the new reagent and the calibrator lot. This in turn means that a change from reagent lot to reagent lot cannot be detected. There may be significant differences between individual reagent lots. This is precisely where the control material, which has not been optimized for the single reagent lot, is required as an independent review of the analytical process.

**Determined cause**

The controls were matched to the reagent lot and thus unable to detect deviations in patient samples.

**Solution**

In the future, independent control materials will be used in the laboratory.

The current RiliBÄK does not provide for independent control [1]. In contrast, ISO 15189 [2] recommends using an independent control

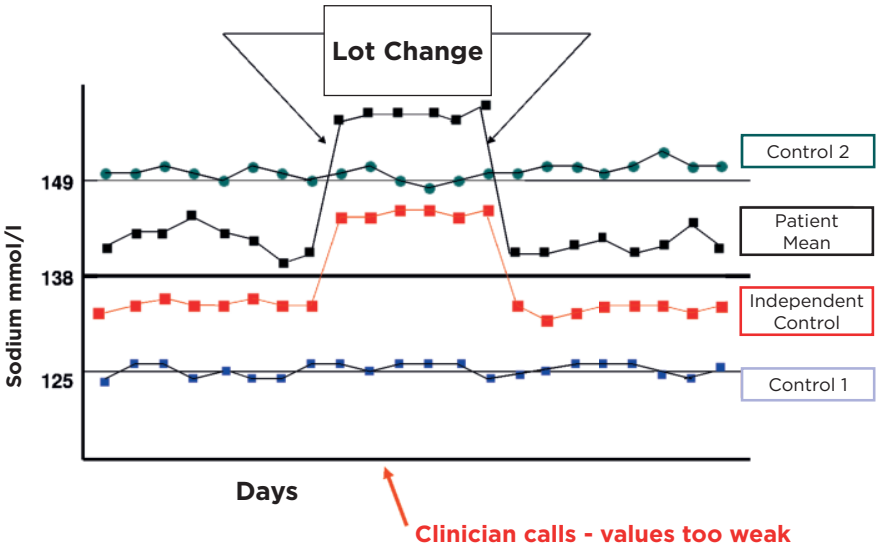
## From the IVDR

CHAPTER III REQUIREMENTS REGARDING INFORMATION SUPPLIED WITH THE DEVICE

20.4.1. The instructions for use shall contain all of the following particulars:

"(u) the metrological traceability of values assigned to calibrators and control materials, including identification of applied reference materials and/or reference measurement procedures of higher order and information regarding maximum (self-allowed) batch to batch variation provided with relevant figures and units of measure;

(v) assay procedure including calculations and interpretation of results and where relevant if any confirmatory testing shall be considered; where applicable, the instructions for use shall be accompanied by information regarding batch to batch variation provided with relevant figures and units of measure;"




*While the control materials of the reagent manufacturer (blue and torquoise) show no deviations, an increase in the sodium measurement values caused by the lot change can be clearly recognized via the calculated patient mean values (black) and the independent control material (red).*

material. Importantly, in the new IVDR [3], the reagent manufacturer is required to report and must, if requested, provide the user with details of the individual reagent lots (see the "IVDR Information" box on previous page).

The monitoring of the performance of the individual lots can only be carried out via an independent control material or by calculating the mean value of the patient results of the respective analyte. However, the calculation of patient mean values depends on many variables and therefore is not always the optimal solution.

Proficiency test samples are also independent control materials, but measurements are not done daily, they are typically at long intervals, as described in the RiliBÄK. This is far from enough considering the case as described at the beginning of this article.

Here the solution is the use of independent control material. Ideally, the control material should be ready for use, i.e. liquid, so that preparation errors can be avoided.

**From the literature**

Miller et al [4] report that an examination of 1483 reagent lot changes on average showed deviations in more than 40.9% (14.3-83.3%) of cases, affecting both quality and response the patient results had an influence.

Another publication [5] described the lot changes in a study that ran for more than 7 years on a collective of supposedly healthy people and diabetics. Again, however, after 7 years at the end of the study, it was concluded that the discovered drift effects were due to lot change and that wrong clinical conclusions had been drawn.

A third case is reported from Italy [6] about a reagent recall for PTH (intact). The control material belonging to the reagent did not indicate the deviation of about 13-45% present. There were about 40,000 results in 18 Italian laboratories affected.

## From the ISO15189

"The use of an independent third-party quality control should be considered either in place of or in addition to the quality control materials provided by the reagent or assay manufacturer."

**References**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