14-15 October 2025

16th Advanced Hemostasis Seminar

Vilnius

Application of Bayesian for QC Management in a Hemostasis Laboratory

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QI.Lab.Med. – Spin-off of the University of Padova

Figure 1 The brain-to-brain loop for laboratory testing 40 years later.

Plebani M. *Am J Clin Pathol* 2011.

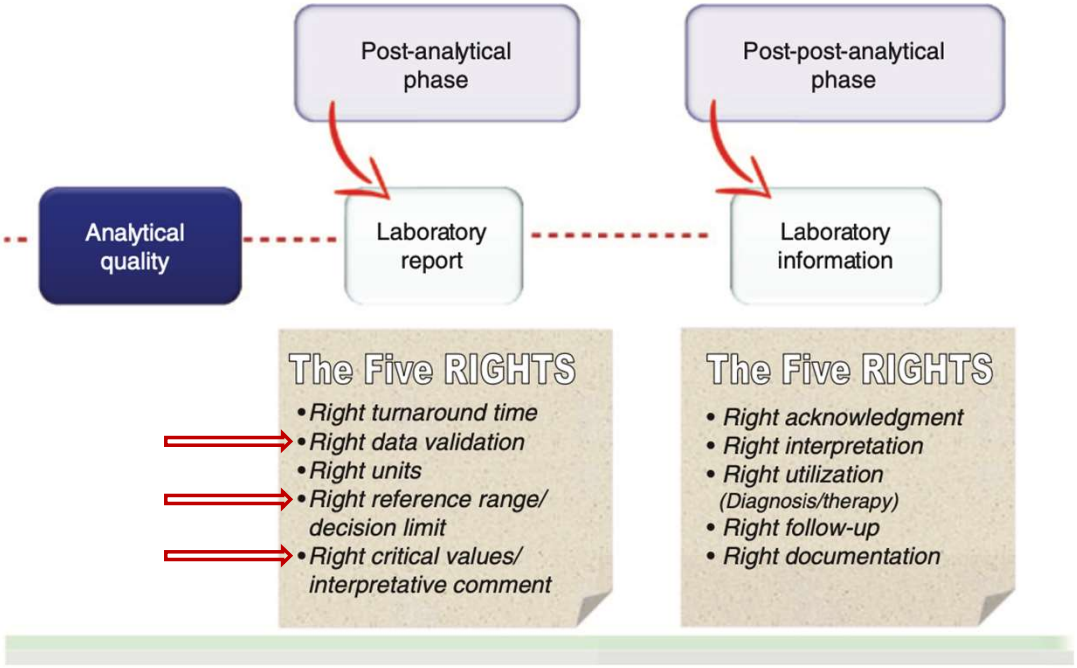


Figure 2: The five rights in the post-analytical phases.

Plebani M. *Clin Chem Lab Med* 2016.

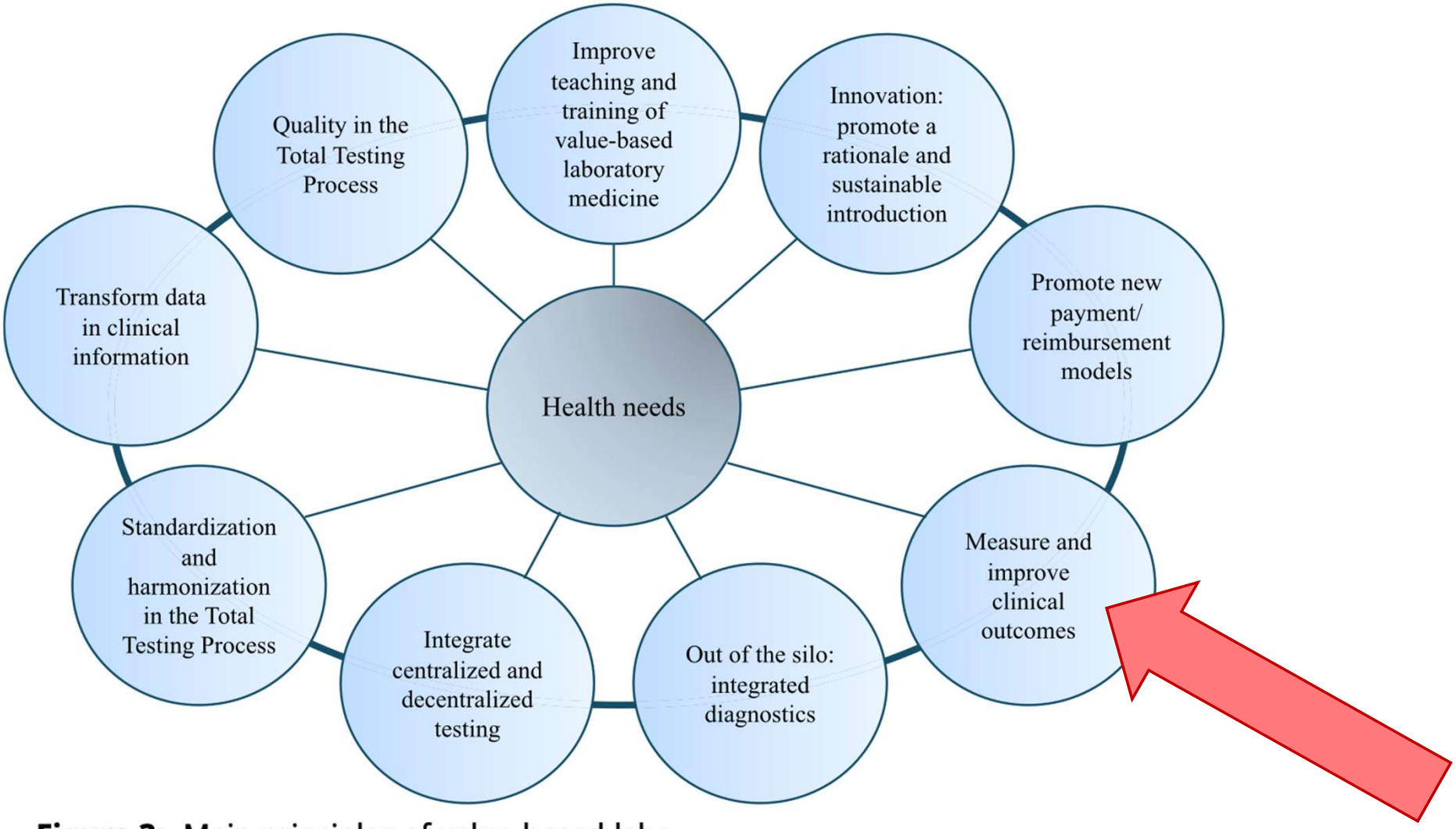


Figure 3: Main principles of value-based laboratory medicine.

Plebani M. *Clin Chem Lab Med* 2024.

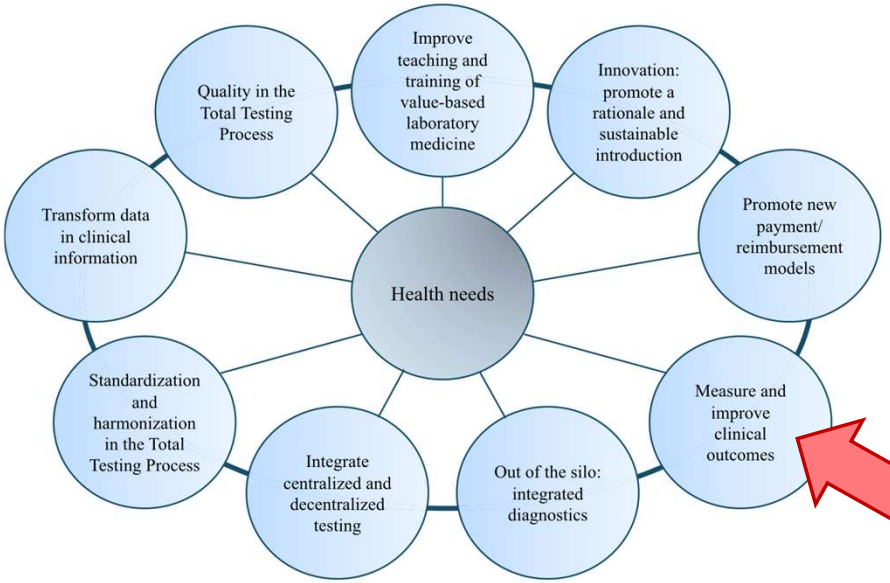


Figure 3: Main principles of value-based laboratory medicine.

Measure and improve clinical outcomes

Porter and Teisberg emphasized the evidence that "there is simply no way to achieve large and sustained improvements in value for patients without measuring results: the set of risk-adjusted outcomes of care for each medical condition, together with the costs of achieving those outcomes "[5]: laboratory professionals have been pioneers in introducing valuable process measurements such as internal quality control (IQC), external quality assurance (EQA), and the model of quality indicators (MQI) in the total testing process [31, 32]. However, processes of care are not results and particularly in laboratory medicine these measures do not provide evidence of benefit nor are they "visible" to users as they are evaluated and documented "within the laboratory walls". Although the relationships between laboratory

Plebani M. *Clin Chem Lab Med* 2024.

DE GRUYTER Adv Lab Med 2022; 3(3): 215–217

Editorial

Mario Plebani*

Internal quality control and external quality assurance: a great past opens the way to a bright future

https://doi.org/10.1515/almed-2022-0075

Keywords: external quality assurance; internal quality control; quality; total allowable error; uncertainty.

Total Error" and the search for quality requirements which should provide an objective guide to method evaluation and utilization in quality control paved the way to a more "clinical-oriented" vision of the IQC. Finally, the proposals

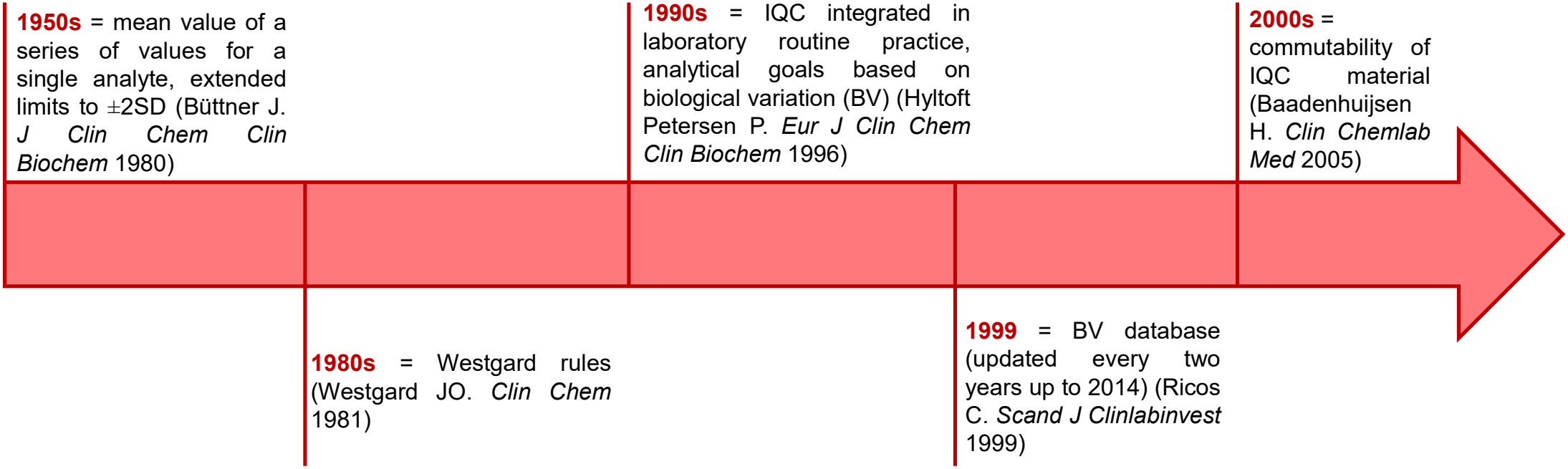
quality and reliability of laboratory results. The authors correctly defined the aim of the IQC as "to monitor the examination process in order to avoid producing erroneous information concerning patient health status" [1], and summarized the roots of the IQC with the following sentence: "the oldest model, developed in the 50s was based on a statistical criterion, from calculating the mean of a number of results from a single measurand in the same control sample. It was supported by the use of a control chart that showed the results of control samples plotted in the X-axis vs. time or day on the x-axis". Thereafter, they moved to describe the significant improvement thanks to the proposal by James Westgard and Coll. of the multi-role algorithm which was implemented in many automatic analyzers [3]. All

Plebani M. *Adv Lab Med* 2022.

IQC = based on a statistical calculation of the mean value of the numbers of results for one single laboratory analyte in the same control material

Ricos C. *Adv Lab Med* 2022.

Bits of history of IQC



Ricos C. *Adv Lab Med* 2022.

CLSI EP26A

User Evaluation of Between-Reagent Lot Variation;
Approved Guideline

5 Performing Reagent Lot-to-Lot Comparisons

As discussed in Section 2, it is recognized that each new reagent lot has the potential to cause a change in patient sample results. Therefore, it is important that each new reagent lot be verified before being put into routine use to report patient results.

How to detect any change?

CLSI EP26A

User Evaluation of Between-Reagent Lot Variation;
Approved Guideline

6 Samples for Reagent Lot Comparability Testing

The goal of evaluating a candidate reagent lot is to verify that any differences in performance between the current and candidate reagent lot are not clinically important for patient samples. As such, the samples tested must represent those used for routine patient testing.

How to detect any difference?

TECHNICAL SECTION

THE USE OF CONTROL CHARTS IN THE CLINICAL LABORATORY*

STANLEY LEVEY, PH.D., AND E. R. JENNINGS, M.D.

From the Departments of Physiological Chemistry and Pathology, Wayne University College of Medicine, and Receiving Hospital, Detroit, Michigan

Constant supervision is necessary in order to obtain uniformly reliable values in a busy clinical laboratory. Normally the director of the laboratory does not have sufficient time to carry out a detailed supervision of the methods but, by the use of control charts, it is possible to determine at a glance whether the errors of analysis are beyond the statistical variation of the procedures employed.

Quality control by statistical methods is widely used in industry[7] to determine whether the variation observed among items produced by a single machine or an entire process is consistent with the hypothesis that a stable system of chance causes is operating. This hypothesis may be tested by taking a number of groups of observations at reasonable intervals of time, to see if the variations among the averages of each group are consistent with the variations observed within groups of observations made at the same time. The details of this technic are furnished by the theory of statistical quality control.[1]

In this laboratory the principle of the control chart provided a constant check on the reliability of the numerous determinations run each day. It made it possible to distinguish between what might be termed statistical fluctuations and actual error. In addition it offered a rational basis for action in correcting a defective procedure. While the chart will show when a method is out of control, *i.e.*, that the variation is greater than would be expected if chance alone were operating, it remains for the analyst to study the cause and prevention of the error. Since control-chart methods have not been widely used in the clinical laboratory, we undertook a study of their application in our laboratory.

METHOD

In setting up the type of control chart used here, it is necessary to have sufficient amounts of homogenous blood or plasma in which the concentration of the material to be analyzed is stable over a long period. Also, the concentration of the substance estimated should be approximately in the range of normal blood values, so that no special analytical steps would be required to check its level.

The pooled blood or plasma derived from this blood was obtained from lots discarded by the hospital blood bank. Whole blood was used to control the urea method, and plasma was used to study the total protein, albumin, globulin and chloride determinations. The blood or plasma was pooled and then distributed as 5-ml. samples in a large number of small test tubes. The latter were well corked, stored in a "deep-freeze" cabinet maintained at −10 C. and kept frozen solid until ready for analysis. Sufficient samples were prepared at this

* Received for publication, May 15, 1950.

A comparison of the 1_{2s} rule and Bayesian approach for quality control: application to one-stage clotting factor VIII assay

Frédéric Sobas[a,*], Panagiotis Tsiamyrtzis[b,*], Norbert Benattar[c], Anne Lienhart[a] and Claude Négrier[a]

Bayesian logic in statistical test control: application to coagulation factor VIII assay

Frédéric Sobas[a], Audrey Bellisario[b], Panagiotis Tsiamyrtzis[c], Anne Lienhart[a], Christophe Nougier[a] and Claude Négrier[a]

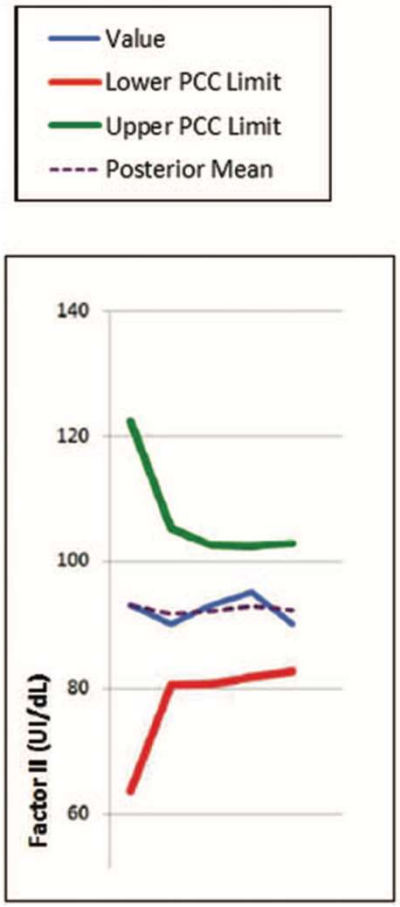
Use of prior manufacturer specifications with Bayesian logic eludes preliminary phase issues in quality control: an example in a hemostasis laboratory

Panagiotis Tsiamyrtzis[a], Frédéric Sobas[b] and Claude Négrier[b]

Determining the adequate number of internal quality control levels: the example of coagulation factor VIII assay

Frédéric Sobas[a], Laurent Mazliak[b], Audrey Bellisario[a], Mathieu Lefranc[a], Anne Lienhart[a], Christophe Nougier[a] and Claude Négrier[a]

Fig. 2



Manufacturer's maximum acceptable coefficient of variation (%)	10
Prior manufacturer's internal quality control value	93
Own inter assay SD estimated at method verification phase	3
Manufacturer's maximum acceptable inter assay SD	9.3

Value	Lower PCC Limit	Upper PCC Limit	Posterior Mean
93	63.680	122.320	93.000
90	80.574	105.426	91.574
93	80.641	102.507	92.034
95	81.683	102.384	92.756
90	82.718	102.795	92.216

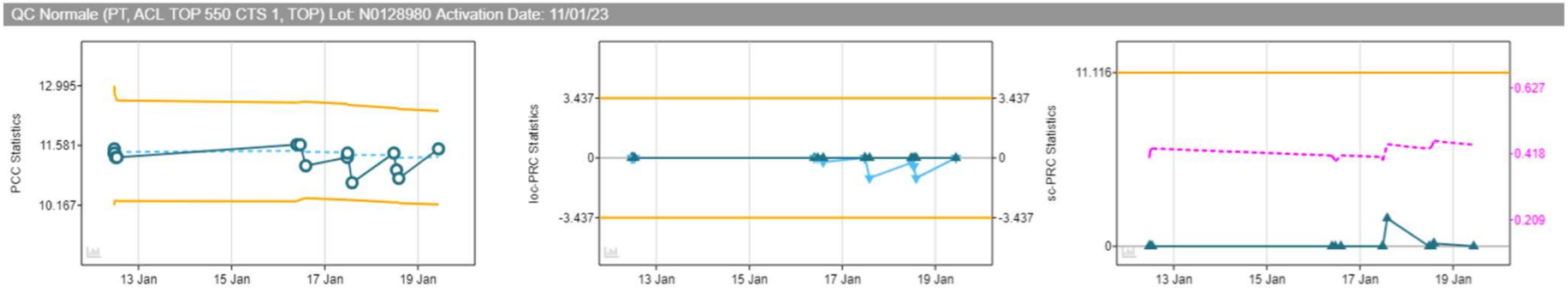
Bayesian statistics is approaching...

Sobas F. *Blood Coagul Fibrinolysis* 2020.

Predictive control chart on normal internal quality control for factor II measurement with optimal performance: that is, own inter assay CV <<< manufacturer's maximum acceptable CV. CV, coefficient of variation.

EXPERIMENTAL PROTOCOL

- Use of two instruments ACL TOP 550 CTS
- Routine coagulation tests: PT, aPTT, QFA
- Analysis of results:
  1. Levey-Jennings control chart (LIS)
  2. Bayesian statistical approach (HemoHub)



PCC = transient shift

loc-PRC = persistent shift in mean

sc-PRC = persistent shift in variance

EXPERIMENTAL PROTOCOL

WEEK 1 – IQC measurements and generation of a stable series of values

WEEK 2 – IQC measurements and generation of a stable series of values + change of reagent lot

WEEK 3 – IQC measurements and generation of a stable series of values with new reagent lot

WEEK 4 – introduction of intentional errors on instrument 1 (PT + aPTT)

WEEK 5 – introduction of intentional errors on instrument 1 (PT + aPTT)

EXPERIMENTAL PROTOCOL

INTENTIONAL ERRORS:

- Resuspension of control material in double volume of milliQ water

EXPERIMENTAL PROTOCOL

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- Use of control material over Manufacturer's declared stability period

EXPERIMENTAL PROTOCOL

INTENTIONAL ERRORS:

- Resuspension of control material in double volume of milliQ water
- Use of control material over Manufacturer's declared stability period
- Use of reagents over Manufacturer's declared stability period

EXPERIMENTAL PROTOCOL

INTENTIONAL ERRORS:

- Resuspension of control material in double volume of milliQ water
- Use of control material over Manufacturer's declared stability period
- Use of reagents over Manufacturer's declared stability period
- Use of control material befor the optimal time after resuspension in milliQ water

EXPERIMENTAL PROTOCOL

INTENTIONAL ERRORS:

- Resuspension of control material in double volume of milliQ water
- Use of control material over Manufacturer's declared stability period
- Use of reagents over Manufacturer's declared stability period
- Use of control material befor the optimal time after resuspension in milliQ water
- Resuspension of PT reagent with a non-precise volume of buffer

EXPERIMENTAL PROTOCOL

WEEK 1 – IQC measurements and generation of a stable series of values

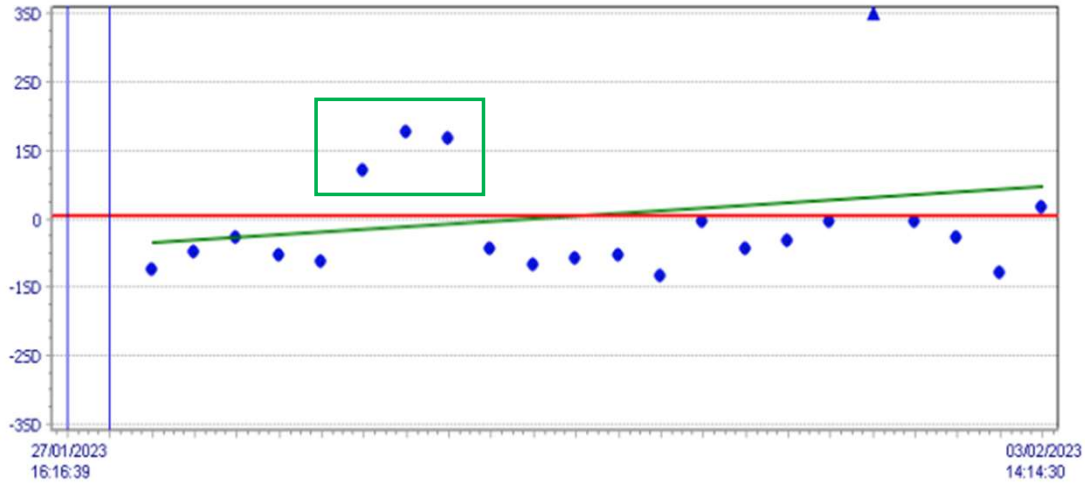
WEEK 2 – IQC measurements and generation of a stable series of values + change of reagent lot

WEEK 3 – IQC measurements and generation of a stable series of values with new reagent lot

WEEK 4 – introduction of intentional errors on instrument 1 (PT + aPTT)

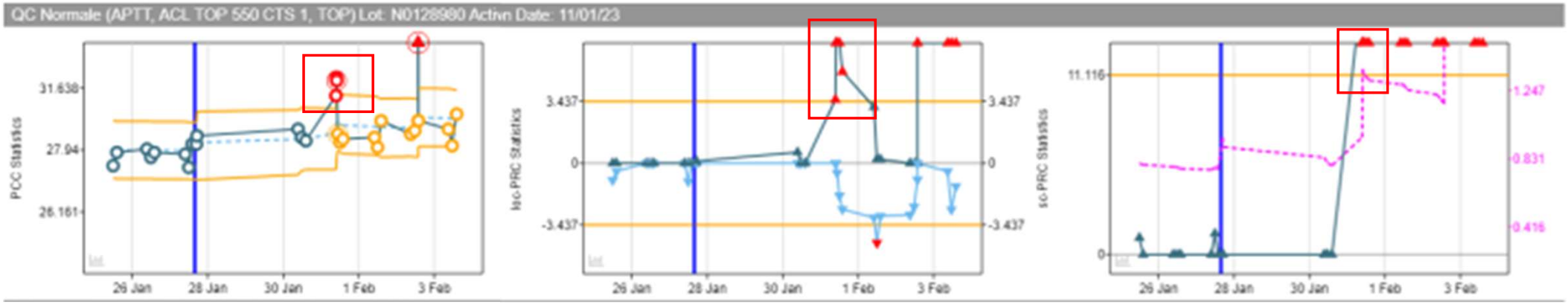
WEEK 5 – introduction of intentional errors on instrument 1 (PT + aPTT)

Normal level aPTT control material



NO erros detected with LJ control chart

ERRORS detected with Bayesian statistics



EXPERIMENTAL PROTOCOL

WEEK 1 – IQC measurements and generation of a stable series of values

WEEK 2 – IQC measurements and generation of a stable series of values + change of reagent lot

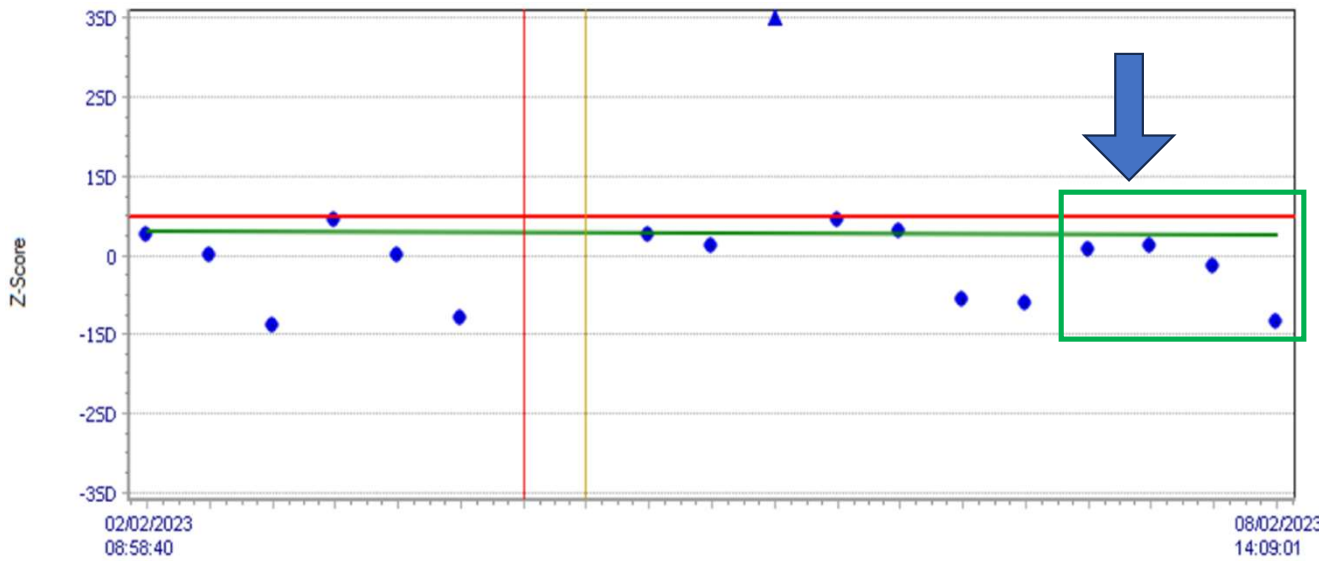
WEEK 3 – IQC measurements and generation of a stable series of values with new reagent lot

WEEK 4 – introduction of intentional errors on instrument 1 (PT + aPTT)

WEEK 5 – introduction of intentional errors on instrument 1 (PT + aPTT)

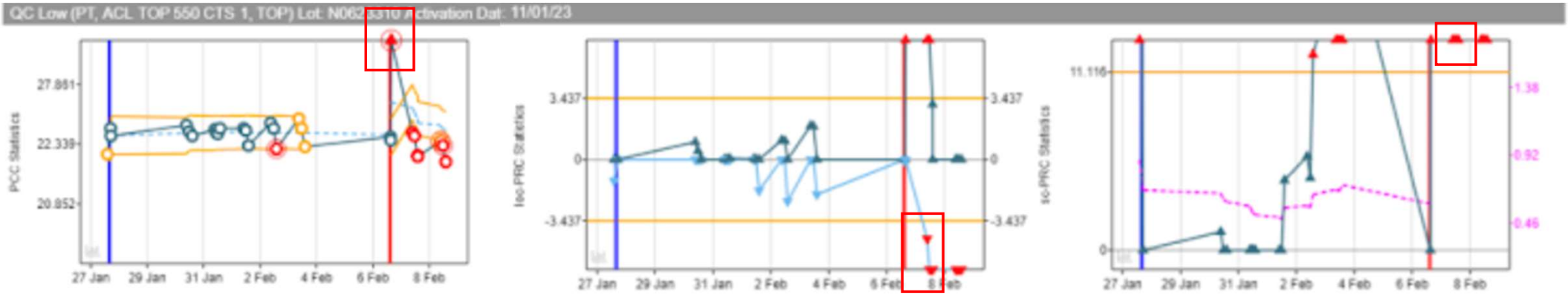
Low level PT control material:

Use of control material after Manufacturer's declared stability



NO erros detected with LJ control chart

ERRORS detected with Bayesian statistics



PRACTICAL QUESTION...

Q: What do I have to do with the errors? Do I have to discard them? How do I know that the system is still working properly?

A: The information that are given by the Bayesian triplet is complementary! One must not focus on one only graph, without looking at the others!

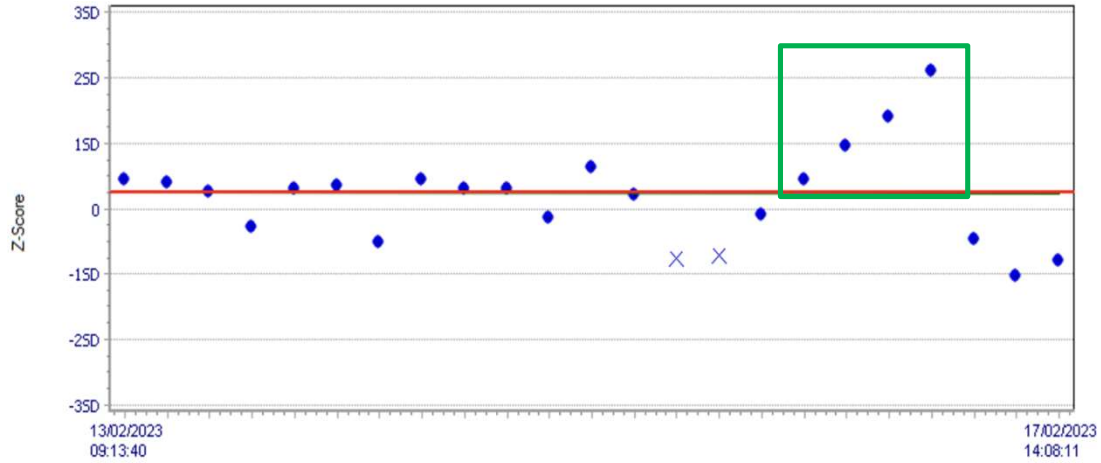
EXPERIMENTAL PROTOCOL

INTENTIONAL ERRORS:

Generation of a **drift** through serial dilutions of control material in milliQ water

1. 400 µL control + 0 µL H2O
2. 400 µL control + 40 µL H2O
3. 400 µL control + 80 µL H2O
4. 400 µL control + 120 µL H2O
5. 400 µL control + 160 µL H2O

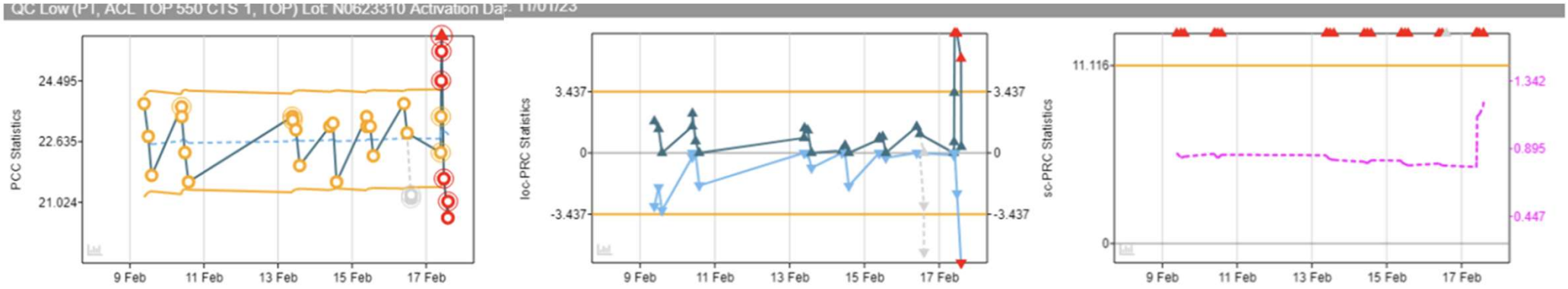
Drif of low level PT control material



Erros detected with LJ control chart

ERRORS detected with Bayesian statistics:

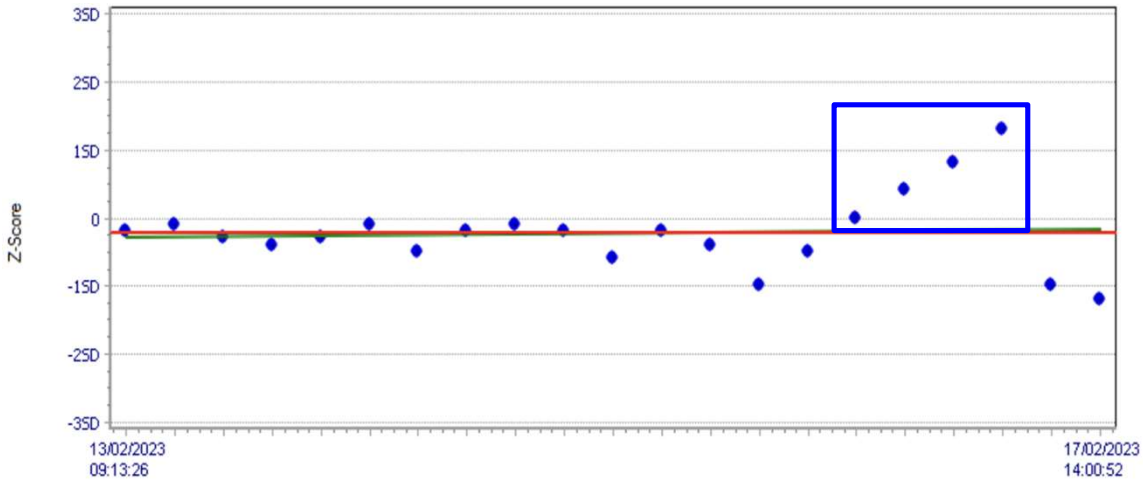
- **PCC**
- **locPRC**
- **scPRC**



Drift low PT

Value (s)	Posterior Mean	Posterior variance	P. Inter-assay SD	Alarms	Comments
22.3	22.7241	0.0083	0.8018	sc-PRC	ctrl + 0 µL H_2O
23.4	22.7465	0.008	0.7989	sc-PRC	ctrl + 40 µL H_2O
24.5	22.8028	0.0077	0.8425	**sc-PRC, PCC**	ctrl + 80 µL H_2O
25.4	22.8835	0.0075	0.9383	**loc-PRC, sc-PRC, PCC**	ctrl + 120 µL H_2O
26.9	23.0046	0.0073	1.1391	**loc-PRC, sc-PRC, PCC**	ctrl + 160 µL H_2O

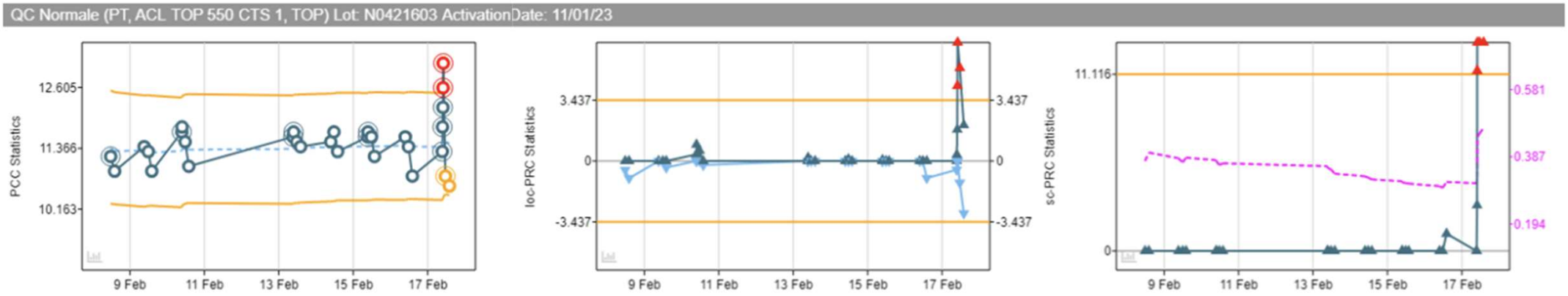
Drif of normal level
PT control material



Erros detected with LJ control chart

ERRORS detected with Bayesian statistics:

- **PCC**
- **locPRC**
- **scPRC**



Drift normal PT

Value (s)	Posterior Mean	Posterior variance	P. Inter-assay SD	Alarms	Comments
11.3	11.3984	0.0043	0.3232		ctrl + 0 µL H_2O
11.8	11.4112	0.0041	0.3238		ctrl + 40 µL H_2O
12.2	11.4356	0.004	0.3418		ctrl + 80 µL H_2O
12.6	11.4705	0.0039	0.3834	**loc-PRC, sc-PRC, PCC**	ctrl + 120 µL H_2O
13.1	11.518	0.0038	0.4569	**loc-PRC, sc-PRC, PCC**	ctrl + 160 µL H_2O

Bayesian statistics for IQC management

Early error detection

Stringent control for lot-to-lot variations in particular diagnostic settings (e.g. hemostasis)

Tool for ISO15189 compliance for traceability after reagent lot change

User-friendly graphical interface

Future developments and studies

University-Hospital of Padova, Italy

IL Spa, Werfen Company, Milan, Italy

questions