The Percentiler and Flagger Programs

Modern quality assurance tools –

web-based monitoring of performance and test stability in relation to the flagging rate as surrogate medical decision

Introduction

The Percentiler/Flagger applications in view of the already existing quality assurance efforts

Short reflections on:

- Internal quality control (IQC)
- External quality assessment (EQA)

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Introduction

IQC is the laboratory's quality assurance backbone; nevertheless, IQC has limitations when commercial samples are used:

- Laboratory performance is only assessed at the peer group level

- Information about assay trueness may be jeopardized by non-commutability issues

- Reagent lot changes may affect control- and patient samples differently

- IQC samples may not be available at medically relevant concentrations

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Introduction

"Ideal" EQA with commutable materials gives information of assay trueness; nevertheless, it also has limitations:

- Materials and logistics are expensive

- Typically EQA is conducted at low frequency which misses effects such as lot-to-lot changes or calibration

- Information for the laboratory is delayed

- "Traditional" EQA with non-commutable samples has the same limitations as IQC

The Percentiler/Flagger programs

Respond to these limitations:

- "Sampleless" web-based programs using data from analyses of patient samples

- "One-time" effort to join

- User interfaces allow dynamic on-line monitoring of mid- to long-term stability of performance and flagging rate

- Demonstrate the influence of factors like lot-to-lot changes or calibration

- Add value to IQC by confirming that observations also apply for patient samples, or revealing missed features

- Peer group comparisons are possible

- Combination of the two programs relates the quality of analytical performance to the effect on medical decision

➡ The Percentiler/Flagger strengthen the laboratory, manufacturer and clinician interfaces

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The Percentiler/Flagger programs

Concept/Design:

- *MySQL database*: built from daily medians of patient results (Percentiler) and % of results flagged against locally used decision points (Flagger)

- *User interface*: shows the moving medians over time for on-line monitoring of the mid- to long-term stability of performance (Percentiler) and the effect of analytical variation on the flagging rate (Flagger)

Analytes covered:

Twenty clinical chemistry analytes
Two thyroid hormones
Recent expansion with 16 analytes: basic hematology, HbA1c, IgG/M/A, ferritin, vitamin B12, folic acid, etc.

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Requirements for the laboratory

Data stratification:

- Instrument or module-specific

- Outpatients

NOTE: Stratification possible with modern Laboratory Information Systems (LIS)

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Requirements for the laboratory

Calculations:

- Instrument- or module-specific daily medians

- Percentage of flagged results (hypo and hyper)
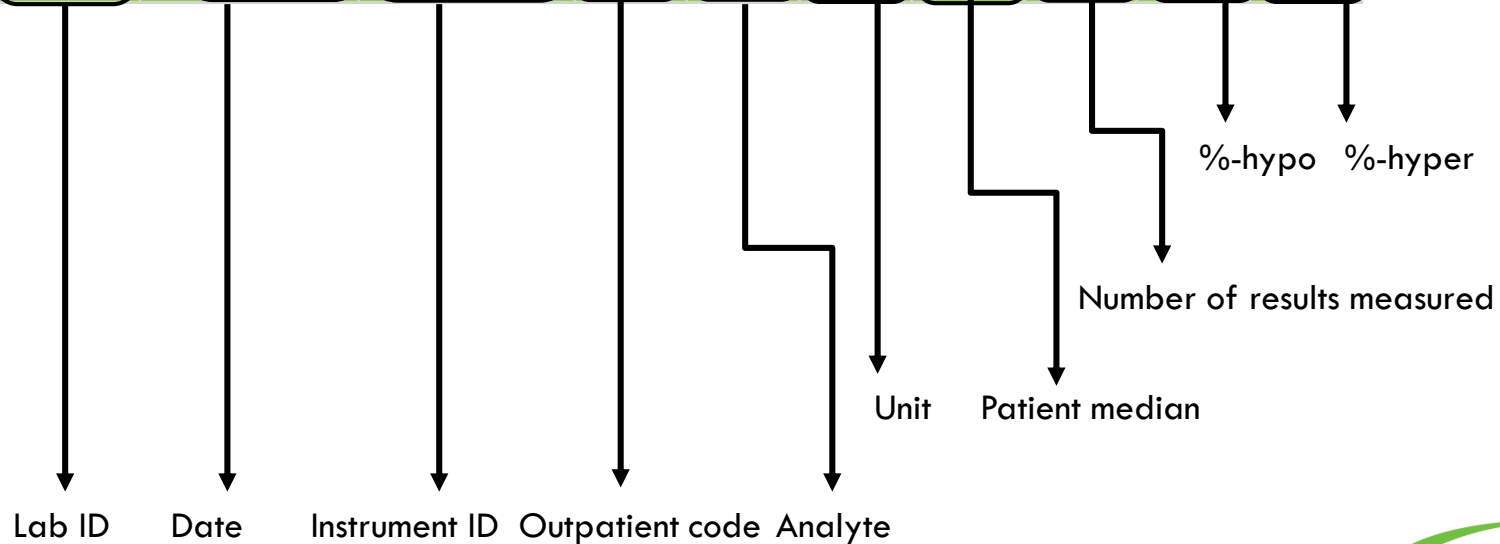
Data transmission:

Electronic transmission of the data to dedicated e-mail addresses (preferably daily, but less frequent reporting is possible)

Currently three formats of reporting possible:
- Embedded in the e-mail
- Attached text file
- Attached Excel® file

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Example of data transmission, Excel attachment to an e-mail

AVDKOD	01.01.2017	COBAS1	PHT	TP	g/L	70.50	6	0	17
AVDKOD	01.01.2017	COBAS1	PHT	TSH	mIE/L	1.60	89	4	0
AVDKOD	01.01.2017	COBAS1	PHT	URAT	µmol/L	301.00	29	3	14
AVDKOD	01.01.2017	ARCHI1	PHT	ALAT	U/L	21.00	134	3	1
AVDKOD	01.01.2017	ARCHI1	PHT	ALB	g/L	46.00	31	0	45
AVDKOD	01.01.2017	ARCHI1	PHT	ALP	U/L	71.00	89	1	6
AVDKOD	01.01.2017	ARCHI1	PHT	ASAT	U/L	22.00	36	3	6
AVDKOD	01.01.2017	ARCHI1	PHT	CA	mmol/L	2.42	47	0	21
AVDKOD	01.01.2017	ARCHI1	PHT	CL	mmol/L	104.00	4	0	0
AVDKOD	01.01.2017	ARCHI1	PHT	CRP	mg/L	1.90	63	0	19

%-hypo   %-hyper

Number of results measured

Unit   Patient median

Lab ID   Date   Instrument ID   Outpatient code   Analyte

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And another example of data transmission

e-mail embedded Table (without *n* and flagging frequencies!)
From: ***
Sent: Saturday, 28 september 2013 06:31
To: percentile@stt-consulting.com
Content: Empower Percentile Project

Time produced : 27-09-2013 00:00 - 27-09-2013 23:59

ABCDEF	27/09/2013	C16000-5	POL	NA	mmol/L	140.9
ABCDEF	27/09/2013	C16000-6	POL	NA	mmol/L	139.4
ABCDEF	27/09/2013	C16000-5	POL	CL	mmol/L	104.6
ABCDEF	27/09/2013	C16000-6	POL	CL	mmol/L	103.8
ABCDEF	27/09/2013	C16000-5	POL	CA	mmol/L	2.44
ABCDEF	27/09/2013	C16000-6	POL	CA	mmol/L	2.42

e-mail embedded Table
From: ***
Sent: Saturday, 21 september 2015 06:31
To: flagger@stt-consulting.com
Content: Empower Flagger Project

Time produced : 27-09-2015 00:00 - 27-09-2015 23:59

ABCDEF;08/04/2015;COBAS8000C1;POL;ALB;g/L;	0%	86%	14%	35
ABCDEF;08/04/2015;COBAS8000C2;POL; ALB;g/L;	0%	87%	15%	37
ABCDEF;08/04/2015;COBAS8000C1;POL;ALT;U/L;	0%	90%	10%	126
ABCDEF;08/04/2015;COBAS8000C2;POL; ALT;U/L;	0%	72%	28%	57
ABCDEF;08/04/2015;COBAS8000C1;POL; CA;mmol/L;	4%	96%	0%	119
ABCDEF;08/04/2015;COBAS8000C2;POL;CA;mmol/L;	6%	94%	0%	102

→ Patient median
→ Unit
→ Analyte
→ Outpatient code
→ Instrument ID
→ Date
→ Lab ID

%-hypo
%-healthy
%-hyper
Number of results measured

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Laboratory IT requirements

Automatic and hassle free calculation and electronic transmission via middleware, Laboratory Information System (LIS) or laboratory self-made solution

- LIS solutions already available: from GLIMS (MIPS), CorLabs (Cegeka), MOLIS (Vision4Health Belgium S.A.), FONS Openlims (STAPRO Ltd.), Modulab (Systelab Technologies, S.A.), Swisslab* (Roche Diagnostics)

- *R-script to extract/send laboratory data from Swisslab at https://github.com/acnb/SwlToEmpower (by courtesy: A. Bietenbeck, MD, PhD, TU München)

Tools provided by the organizers

Software and MySQL database

- Mapping of laboratory-specific codes (for laboratory ID, instruments, analytes)/units
- Automatic reading of e-mails and transfer to the database
- Grouping of laboratories in peer groups

Graphical user interfaces

- Accessible with laboratory-specific login/password
- Show instrument- or module-specific moving medians in time (of the individual laboratory; peer group)
- Show zones for stable performance/flagging based on quality goals

Peer group overviews

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Quality goals

Percentiler:

- If possible, based on biological variation
  - e.g. for total cholesterol, allowable bias 4% (0.2 mmol/L at a median of 4.90 mmol/L)
- If not feasible (e.g., for analytes with tight biological control), bias goal based on state-of-the-art performance

  - e.g. for sodium, 0.7% (1 mmol/L at a median of 140.6 mmol/L)

Flagger:

Analyte-specific limits expressed *relatively* to the long-term flagging rate, but with an absolute minimum of 1%; e.g., for AST the limit is set at 30%:

  -If the flagging rate is 10%, limit = ± 3% (30% of 10%)
  -If the flagging rate is 2.5%, limit = ± 1% (NOT 0.75%)

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User interface – Percentiler

https://www.thepercentiler.be

Login: User = DEMOLAB, password = demo1234
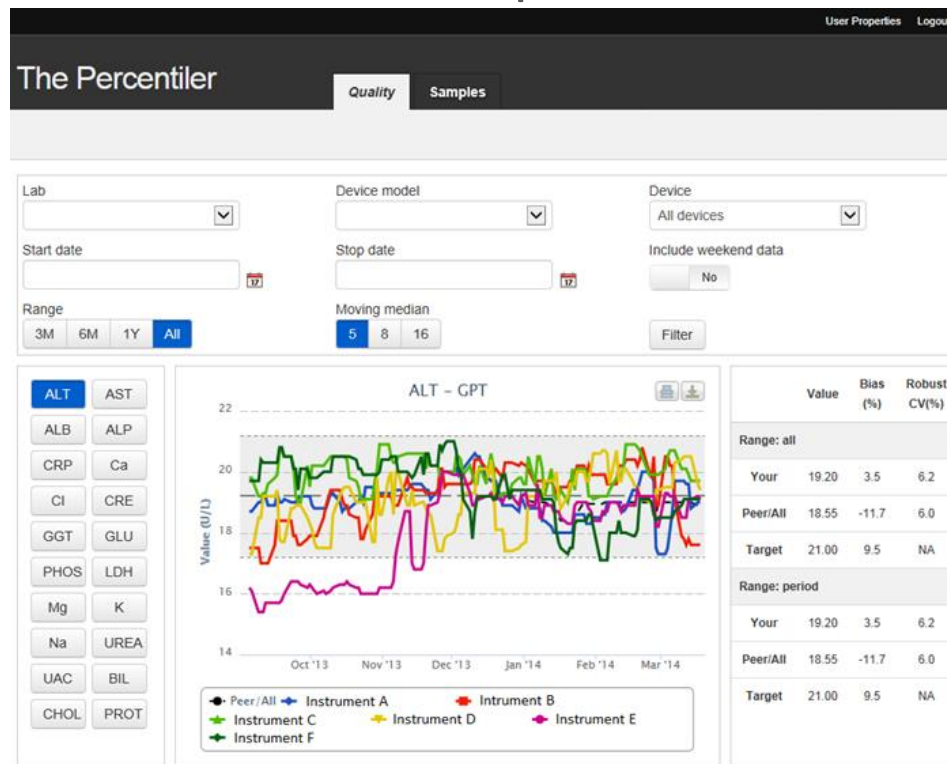
User interface – Percentiler
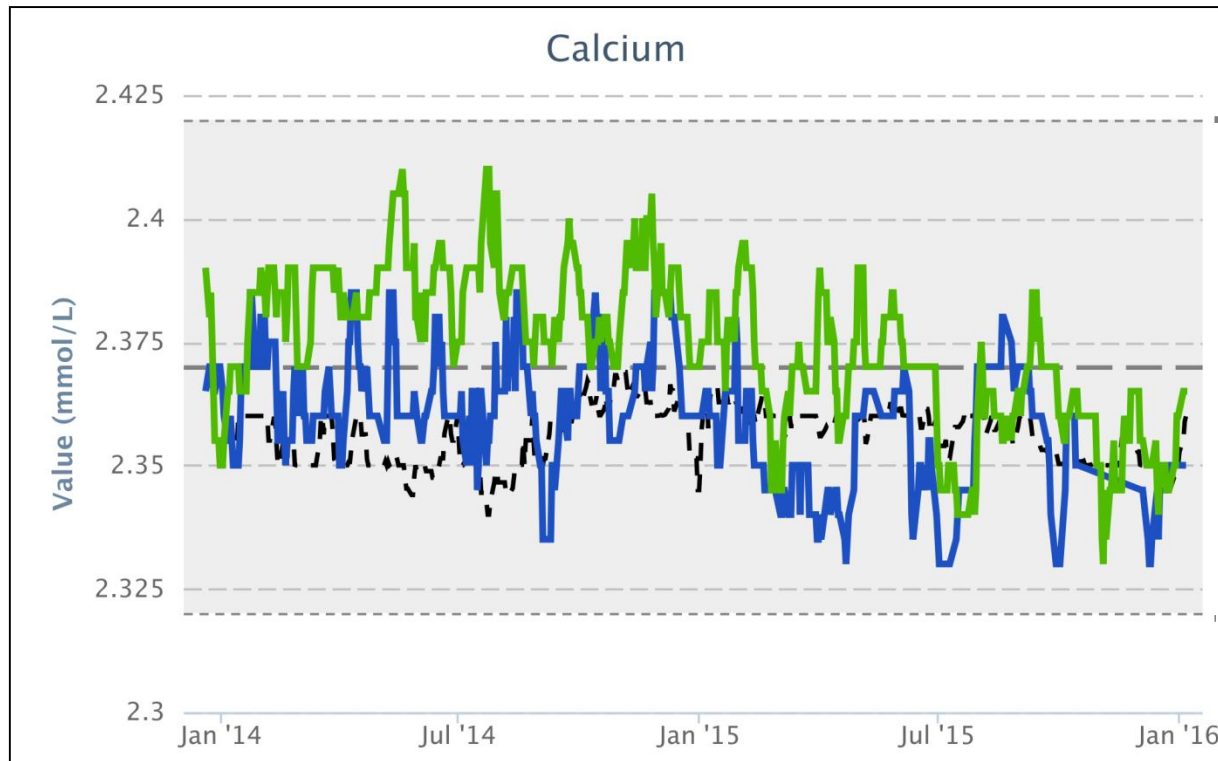
The shaded zone reflects stable performance; the limits ----- around the long-term median are the bias limits; in the calcium example they are at the median $\pm$ 0.05 mmol/L or 2.1%

Legend:

Moving median from Jan 2014 til Jan '16 for two instruments in a laboratory.
Grey dotted line: the laboratory's long-term median.
Black dotted line: the peer group moving median.

NOTE: plots can be downloaded by users.

Percentiler – selected examples

Identifies stable performance for calcium in the selected laboratory and peer group (see the moving medians within the limits of the stability zone)

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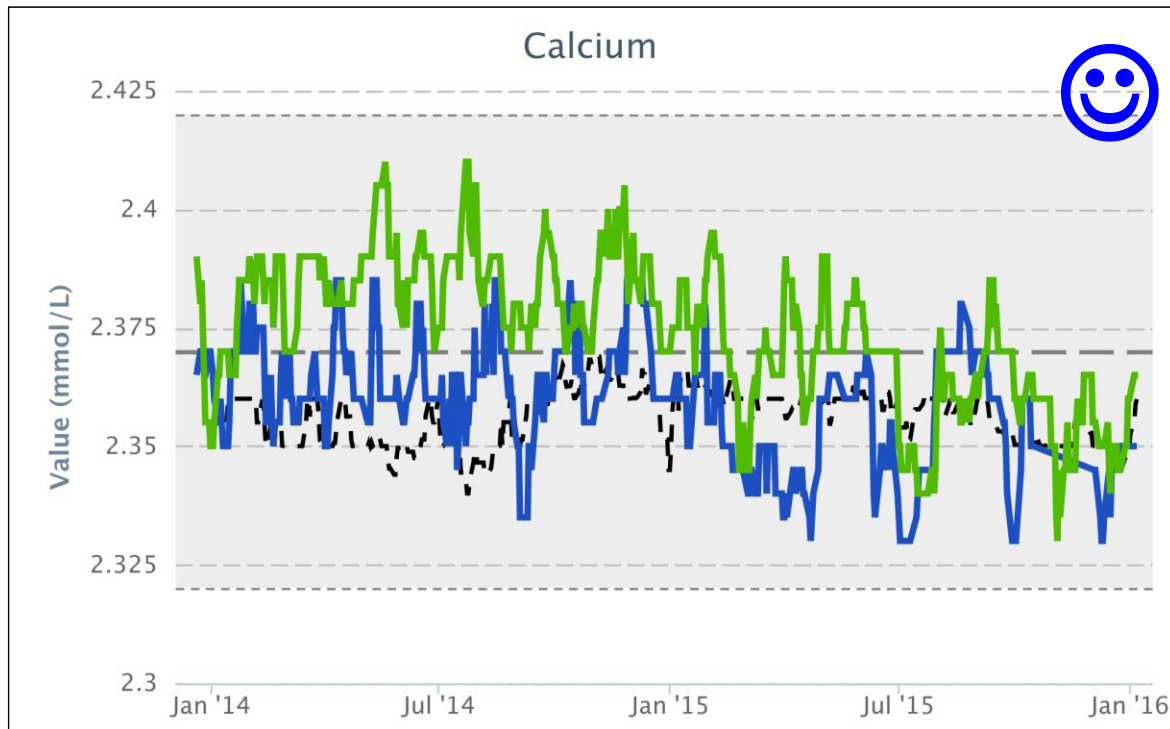
Percentiler – selected examples

Identifies unstable performance for ALT–GPT in the selected laboratory and peer group due to the effect of lot-to-lot changes (see the shifts of the moving medians outside the limits of the stability zone)
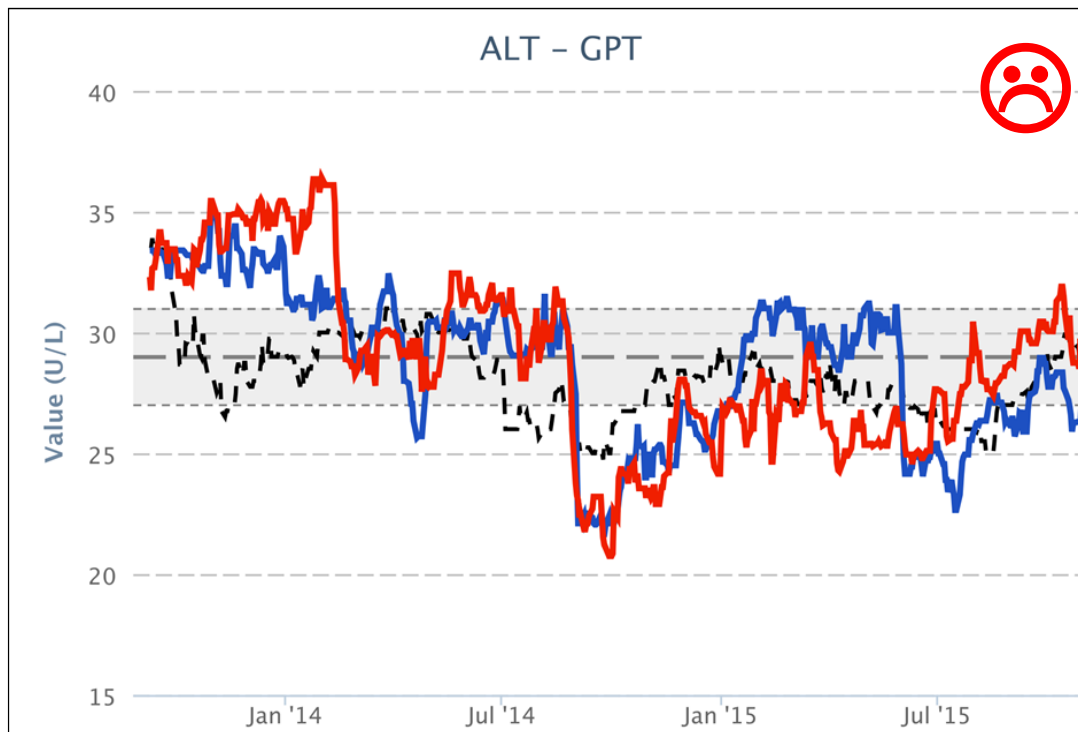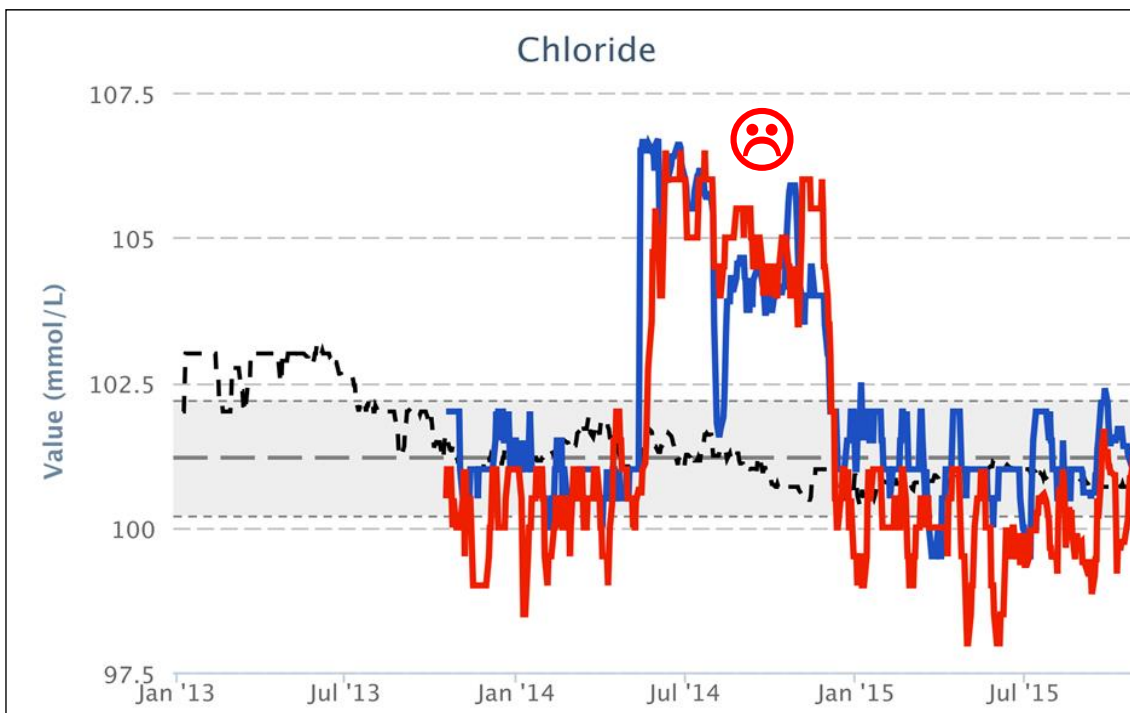
Percentiler – selected examples

Identifies unstable performance for total-protein in the selected laboratory due to reagent instability requiering recalibration (see the typical saw tooth pattern of the moving median)
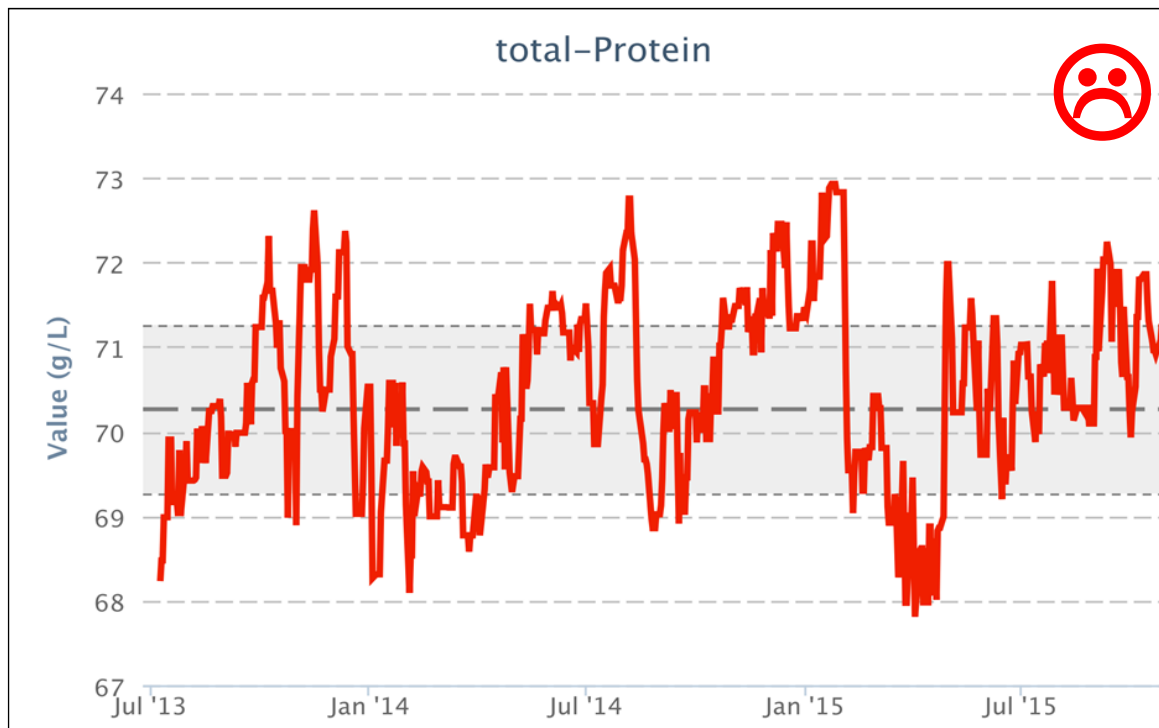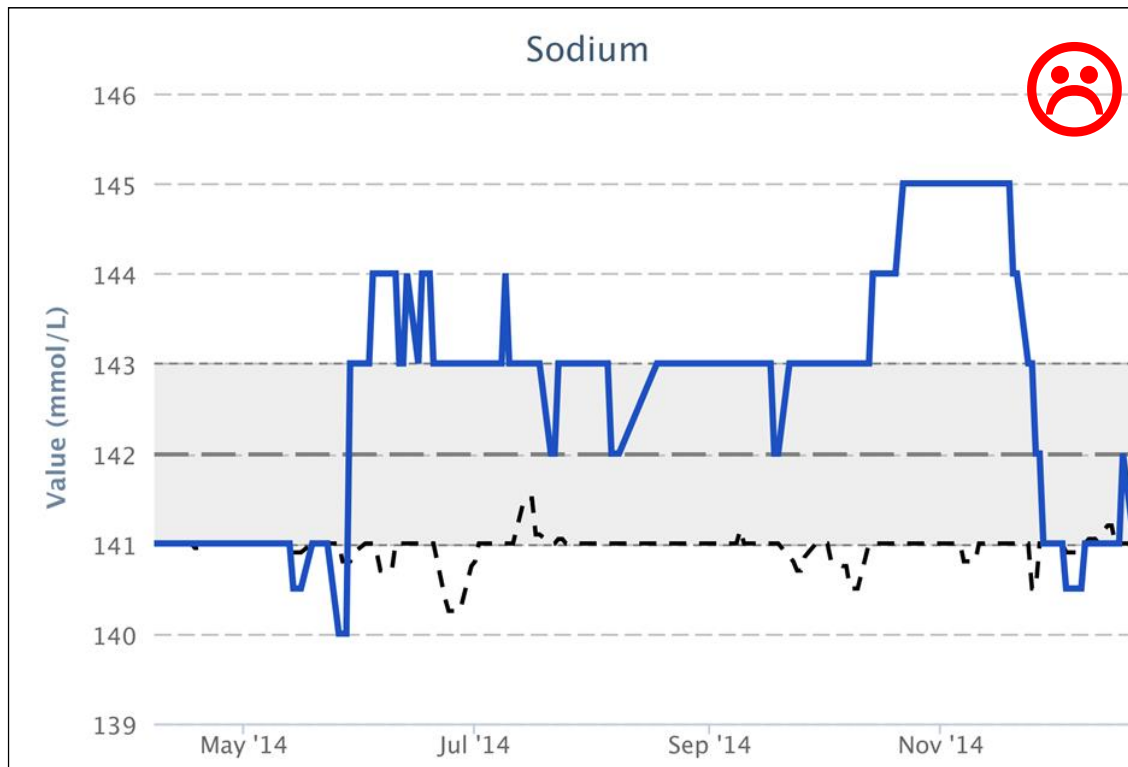
Percentiler – selected examples

Identifies unstable performance for chloride in the selected laboratory (peer group not affected) due to electrode deterioration and recalibration (problem solved after electrode replacement)


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Percentiler – selected examples

Identifies that the selected laboratory is biased relative to the peer group for sodium
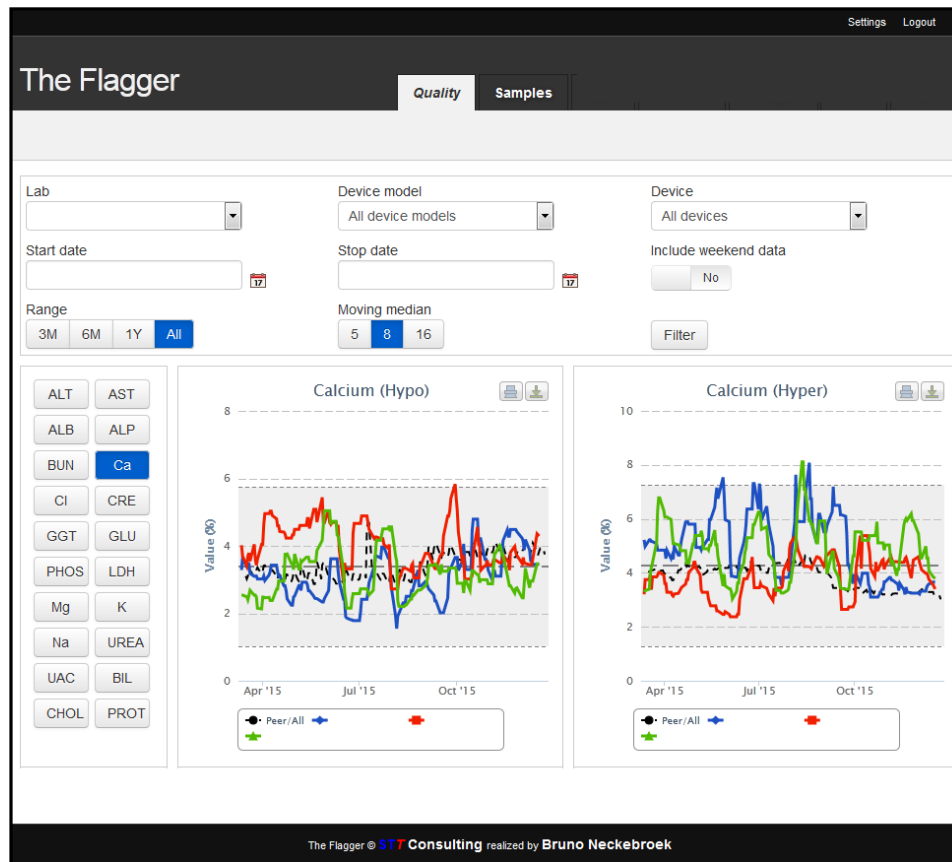
Percentiler – selected examples

Demonstrates poor preanalytics for potassium (the effect of the temperature on the medians: high in winter, low in summer, opposite to the temperature)
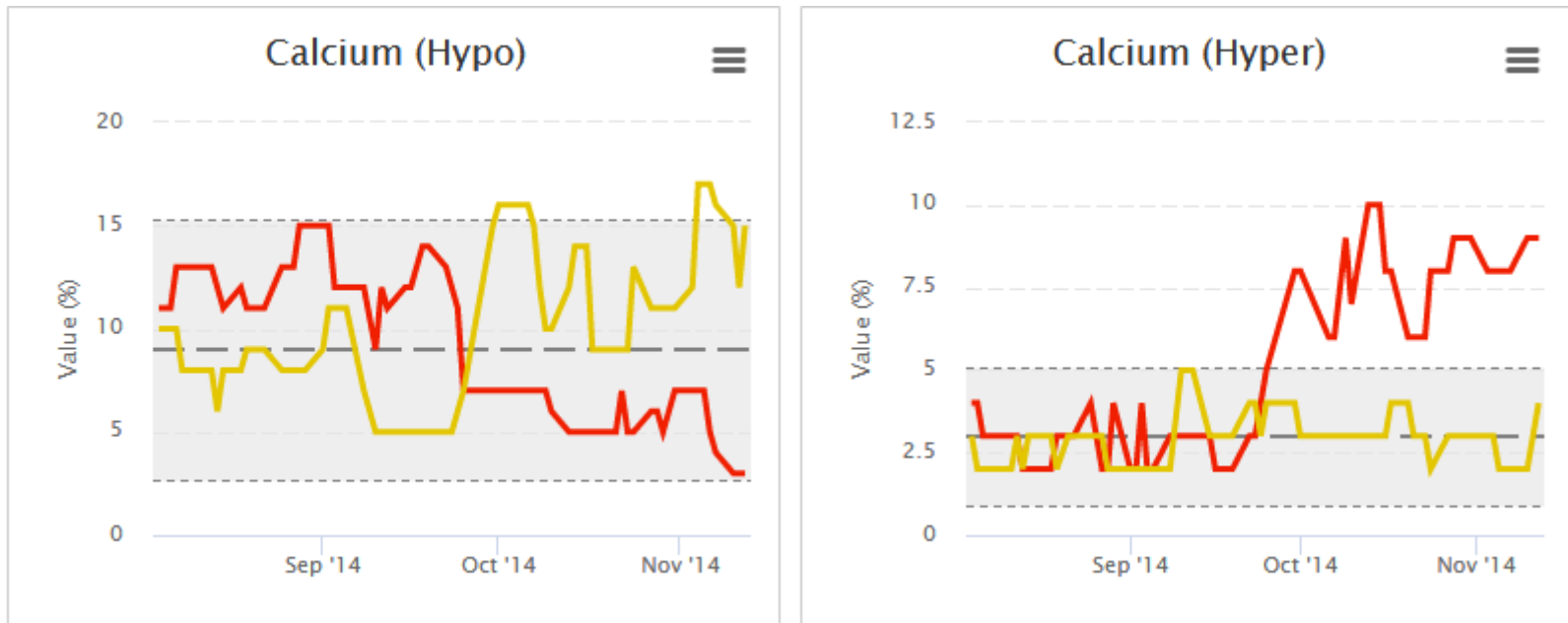

Potassium (red)/Inverse Temperature (Blue)

User interface – Flagger

https://www.thepercentiler.be
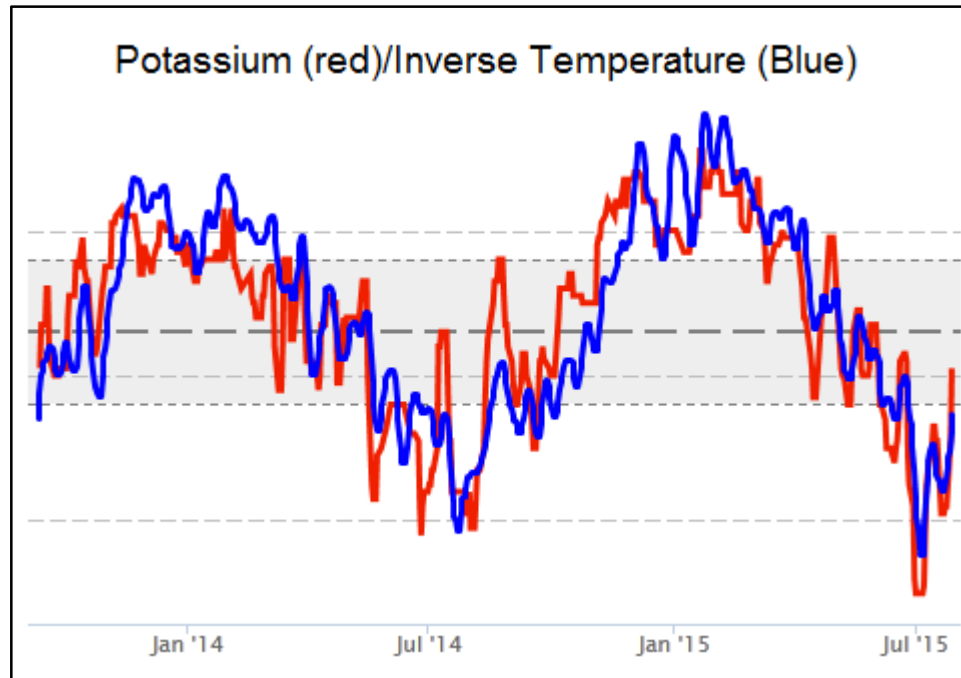
Login: User = DEMOLAB, password = demo1234

User interface – Flagger

Legend:

——— (red)	Moving median of % hypo and hyper flagging rate from July 2014 to Nov '14 for
——— (yellow)	two instruments in a laboratory.
– – – (grey)	Grey dotted line: the median of the laboratory's long-term flagging rate.

The shaded zone reflects stable flagging rate; for the calcium example the limits ----- of the zone are at ± 70% of the median for the long-term flagging rate.

Percentiler & Flagger synergy

Demonstrates the effect of analytical instability on the flagging rate as surrogate of medical decision
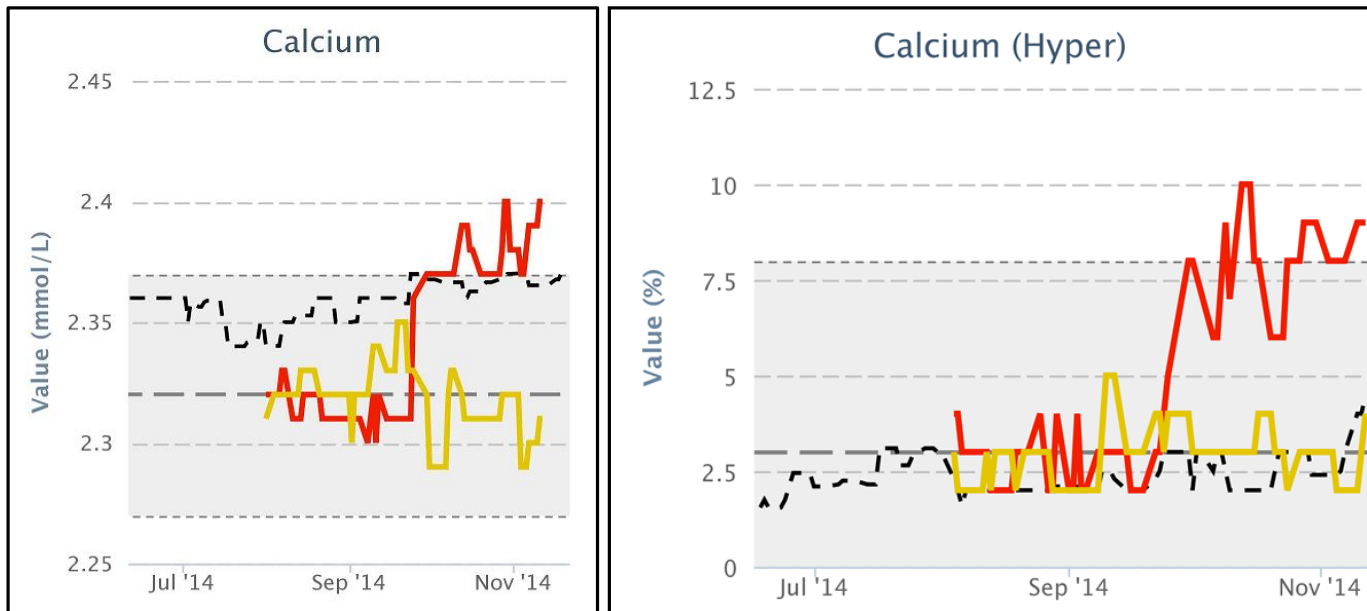
Explanation:
-Left hand plot in the Percentiler; the yellow instrument has stable performance for calcium; in contrast, the red one shows a shift of ~0.06 mmol/L.
-Right hand plot in the Flagger: the hyper flagging rate for the yellow instrument is stable, while for the red one it is triplicated (median from 2.5% to 7.5%).

The way forward

Hosting of the programs by NOKLUS:

- Further development by IT programmers

- Confidentiality ensured (agreement can be made)

- Establishment of an international advisory group

- Meetings with users to better address their needs

- Discussion of the role of the programs for IQC/EQA with specialists in laboratory medicine, national EQA organisers and through the EQALM platform

- Linda Thienpont/Dietmar Stöckl (Thienpont & Stöckl Wissenschaftliches Consulting GbR) will be our consultants on the programs and aid with further development

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Percentiler and Flagger Programs

Interested?

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References

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