

New EQA program – Few analytes but many single donation samples & Virtual EQA – Real-time monitoring of Norwegian clinical laboratory data

NKK Møtet
Trondheim, March 16 2011

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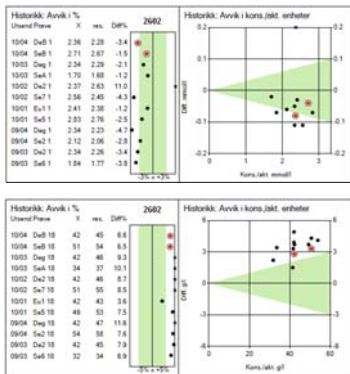
New EQA



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New EQA – Why?



Calcium (top) & Albumin

Many laboratories show persistent bias in NKK surveys

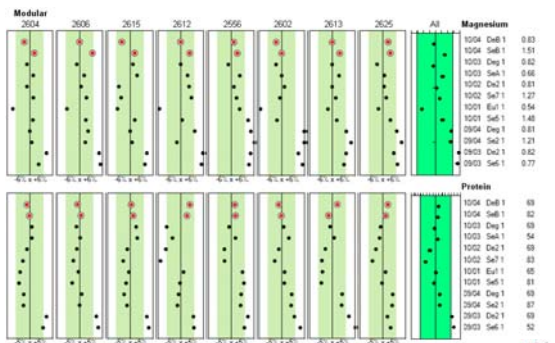
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New EQA – Why?

Many laboratories follow similar trends (manufacturer?)



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New EQA – Why?

It seems that laboratories do not act on EQA-results

Traditional EQA has reached a point where further progress seems difficult

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New EQA

Central questions

- Do we need improvement at all?
- What is “good enough”?
- Can it address problems traditional EQA cannot?

We think yes



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New EQA – How?

Fresh frozen samples CLSI 37 protocol

>Commutable (~16 000 \$, sponsored by Gent)

Single donations

>Assessment of total error

20 samples (2 times 1 mL aliquots)

>Reliable outcome, but “one point in time”

Homogeneous groups with sufficient n (≥ 5)

(Abbott, Ortho, Roche, Siemens)

>Strictly separate manufacturer- and laboratory effect

Targets for pilot survey: homogeneous assays

>Cost effective & reliable for selected analytes

Analytes: calcium, magnesium, albumin, protein

>“Benchmark” analytes, build system up from bottom

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New EQA – How?

Measurement

- All 4 analytes, randomized in 1 run, in singlicate
- Repeat the other day
- Report “original” & recalculated results, when applicable

Additional samples

Typical EQA-samples for assessment of commutability

Information from lab

- Assay
- Calibrator lot
- Reagent lot
- Reference interval (40 year-old men)

Time

April (samples are currently prepared)

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New EQA – General data analysis

Standardization

Manufacturer means of homogeneous groups

Overview of results

Laboratory averages

Bias

Histogram of laboratory biases

Total error

Histogram of laboratory correlation

Number of samples outside TE-limit

“Clinical”

Results outside reference interval

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New EQA – Data analysis laboratory

Imprecision

Duplicates

Bias (overall & concentration-dependent)

- *t*-test
- Regression

Total error

Difference plot & residuals plot

Reference interval enlargement/compression

Slope-test

“Clinical”

Results outside reference interval

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New EQA – Which limits?

		Albumin	Calcium	Magnesium	Protein
Bias-limit	CVw	1.0	0.6	1.2	0.9
Bias-limit	CVg	1.3	0.8	1.8	1.2
TE-limit	NKK	5.0	3.0	6.0	5.0
TE-limit	Westgard	3.9	2.4	4.8	3.4
	CVw	3.1	1.9	3.6	2.7
	CVb	4.2	2.8	6.4	4.0
	CVg	5.2	3.4	7.3	4.8

Will be discussed in “Virtual EQA” part

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New EQA – Data analysis laboratory

Demo EXCEL-file



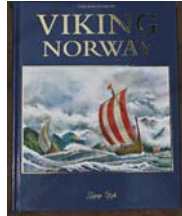
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Virtual EQA

Codename
"The Viking-project"



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Virtual EQA – The idea

Why do "physical" EQA at all?

- Low frequency
- Data too late to act upon (survey "response-time")
- Sample commutability
- Surrogate for what one really intends to assess, namely, the performance for patient samples

Why "Virtual EQA"

- Data are already available in the laboratory (patients' results)
- Real-time
- Direct assessment

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Virtual EQA – The practice

Data

Laboratories send once a week (for example Friday) the daily 10th, 50th, 90th percentiles and the number of results of their patients' data to a central point (no weekends, no holidays).

Recommended calculation: $p(k) = (k - 0.5)/n$.

Information from lab

- Assay
- Instrument
- Calibrator lot
- Reagent lot
- Reference interval (40 year-old men)

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Virtual EQA – Pilot study

Analytes

"Benchmark analytes": *greatest stability expected*

- Sodium
- Chloride
- Calcium
- Magnesium
- Albumin
- total-Protein

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Virtual EQA – Pilot study

Laboratories

≥ 5 laboratories, each:

- Abbott
- Ortho
- Roche (Modulars, only)
- Siemens (Advia's, only)
- Others welcome

Only those manufacturers have a significant number of systems on the Norwegian market. Other laboratories are welcome, but manufacturer effects cannot be investigated.

Note: It would be highly desirable to start the pilot with 1- or 2-year retrospective data.

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Virtual EQA – Data analysis

Data analysis

- The data are accumulated for each individual laboratory and analysed by adequate statistical techniques for "location" and stability (moving averages, %-ages > or < cutoffs, for example); the most appropriate data treatment techniques may emerge after a time of experience (1 year).
- Laboratories with the same assay (maybe even with the same lot numbers) are grouped to extract assay-related information (within-lot stability; lot-to-lot variation; calibration bias).
- After some time, evidence is built up about the consistency of Norwegian laboratory data in terms of manufacturer effects and in terms of laboratory effects.

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Virtual EQA – Benefits

Laboratory

- Comparison of performance with other laboratories
- Information about medium- to long-term assay stability
- Establishment of quality goals for lot-to-lot variation → **approach industry/IFCC**
- Improved calibration and stability of new assays

Society

Laboratory data usable for support of public healthcare policies

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Virtual EQA – Obstacles

Software

Software structure may not allow easy data calculation and transfer.

Questionnaire results

12 responses, 8 calculate medians, but the use thereof is limited, typically no long-term investigations.

Patient data

- Variation in patient data may be too high to identify assay effects (particularly for low-volume laboratories and low-volume tests).
- Patient populations may be different in different laboratories which may confound estimates of analytical biases >back-up by IQC data?

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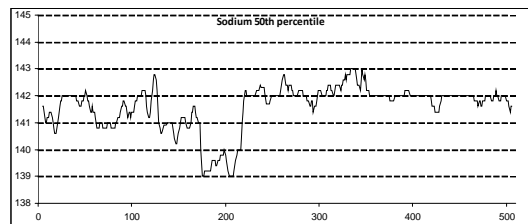
Virtual EQA – Example

2 years data from Fürst

Sodium example, moving average n = 5

Average: 141.6 mmol/L

Maximum deviation 2.6 mmol/L ~2%: similar to 2 other laboratories over a period of 10/13 years.



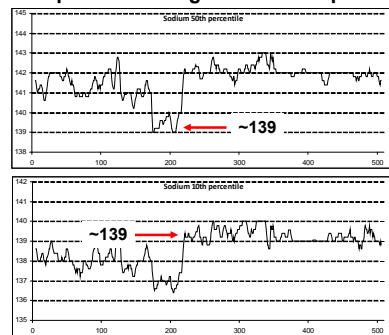
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Virtual EQA – Example

Sodium, 10th & 50th percentile

Comparison of “high” and “low” phases



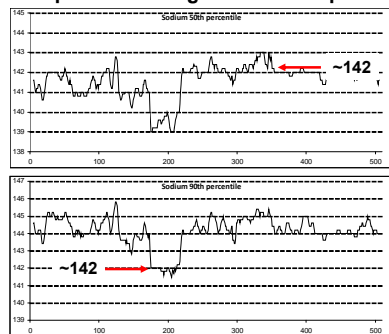
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Virtual EQA – Example

Sodium, 90th & 50th percentile

Comparison of “high” and “low” phases



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Virtual EQA – Example

Sodium, data from other laboratories

Comparison of “high” and “low” phases

Classification of mild hyponatremia (<135 mmol/L) may drastically increase from “high” phases to “low” phases!

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Quality specifications

Sodium data

Are the changes of ~2% relevant?
In my opinion, yes!

Within subject biological variation = 0.7%
>Maximum shift/drift: $\frac{1}{5}$ = 0.2%

Group biological variation = 1.2%
>Maximum bias: $\frac{1}{4}$ = 0.3%

“Realistically desirable” in my opinion

1 mmol/L stability = ~0.7%

Note: this was achieved by 1 lab over 7 years!

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Quality specifications

Questionnaire “QC-acceptance criteria”

Question not precise enough, many sent values for
“stable CV” (red); Intention: limit for shift/drift control!

S-sodium	S-protein	S-albumin	S-phosphate	S-calcium	S-magnesium
0.9	1.6	1.4	1.3	1.5	4
1	1.4	1.6	2.1	2	2.1
0.8	2	1.9	2	1.9	2
1	1.6	2	3.2	2.2	1.8
1.5	2	2	3	2	2
1.8	3.7	2.9	6.3	2.5	3.8
1.4	2.5	3.3	3.2	2.5	2.2
1.4	4.1	4.7	4.4	5.1	5.7
3	6	5.5	7.7	5.3	7
1.8	4.5	5.8	6	4.8	2.8
2.5	5.6	6.7	7.5	4.5	5.0
3.1	6.0	6.9	6.0	4.8	7.7
2.1	4.6	5.1	5.9	4.2	4.9

Mean “black”

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Quality specifications

Questionnaire “Desirable lot-to-lot variation”

Most use bias data from Westgard page ($\frac{1}{4}$ CVg#)

(#My CVg different from “Westgard” CVg = between, only!)

S-sodium	S-protein	S-albumin	S-phosphate	S-calcium	S-magnesium	
0.2	0.9	1.0	2.8	0.6	1.2	0.33 x CVw
0.3	1.2	1.3	3.2	0.8	1.8	“Westgard”
0.3	1.2	1.3	3.2	0.8	1.8	“Westgard”
0.3	1.2	1.3	3.2	0.8	1.8	“Westgard”
0.3	1.2	1.3	3.2	0.8	1.8	“Westgard”
0.4	0.9	0.7	1.8	1.0	1.7	
0.5	1.4	1.6	1.5	1.7	1.9	
0.3	5.0	5.0	4.8	3.0	2.8	
4.0	4.0	4.0	4.0	4.0	4.0	“Roche-rule”

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In the end

In the end, it all will depend
on the quality specifications chosen!



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