USING TOTAL ERROR TO:
- MONITOR PERFORMANCE,
- QUALIFY REAGENTS AND CALIBRATORS, AND
- SELECT QC PROTOCOLS

REAL WORLD EXAMPLES

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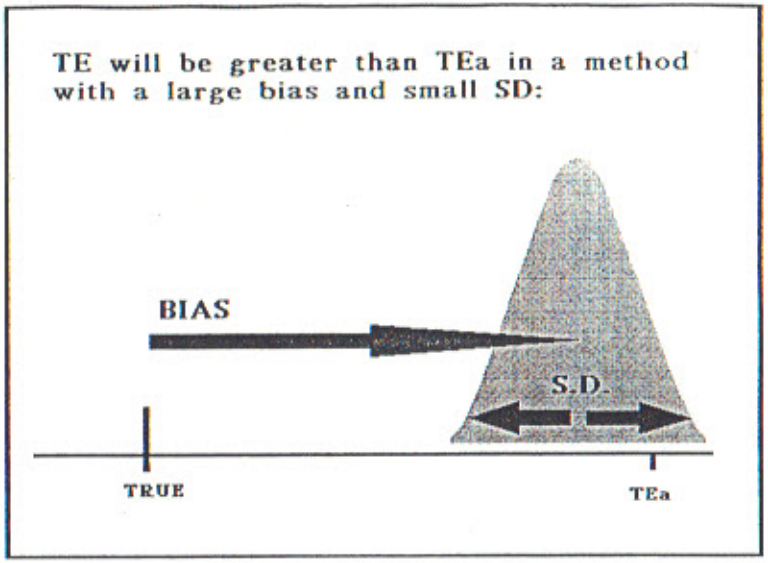
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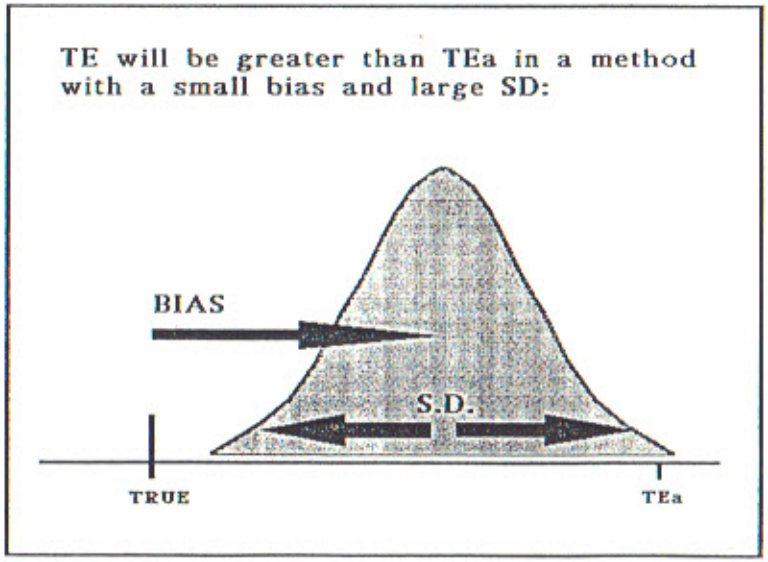
New York City
July 15, 1993

INTRODUCTION

In a poster presented at AACC in 1992, we demonstrated that comparison of Total Error (TE) to a clinically-determined Total Allowable Error (TEa) is a simple and effective way to monitor changes in QC performance and to predict the acceptability of new lots of reagent and calibrators.

Here we apply this theory further in real-world examples to evaluate monthly QC, assess new lots of reagents and select appropriate QC rules.



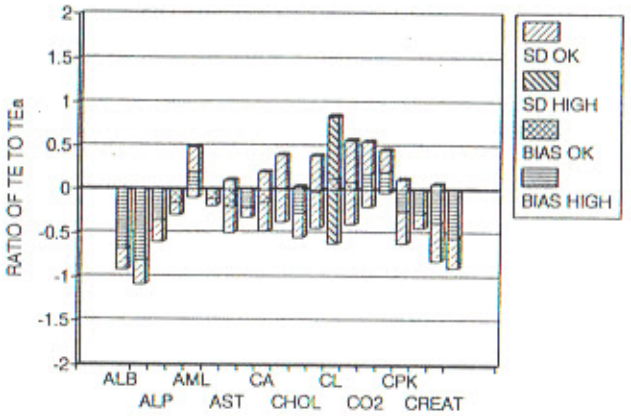


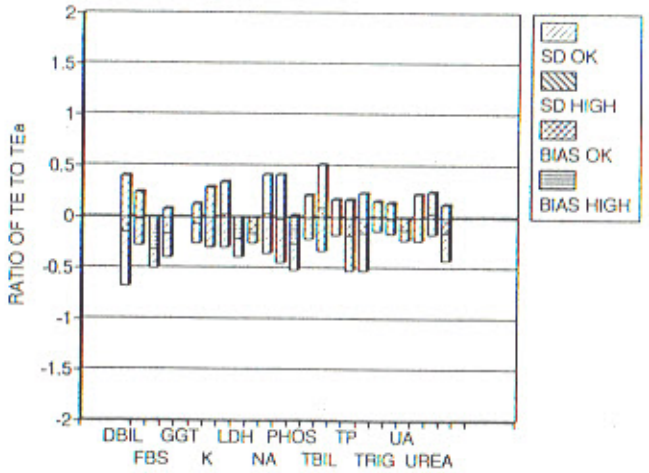
MONTHLY QC

Routine daily QC was performed in six hospital laboratories using Dade controls in chemistry, blood gas, coagulation, special chemistry and hematology. The transmitted interlab report was imported into Paradox . Data were exported to Quattro Pro to create graphs showing the ratio of TE (IBiasI + 1.96 x SD) to the clinically acceptable TEa set by G. Massarella for each test/control.

If TE was greater than TEa, tests were flagged and investigations performed using the TE Flowchart.

CHEMISTRY LAB X JUNE 1993





EXAMPLES

TOTAL ALLOWABLE ERROR LIMITS

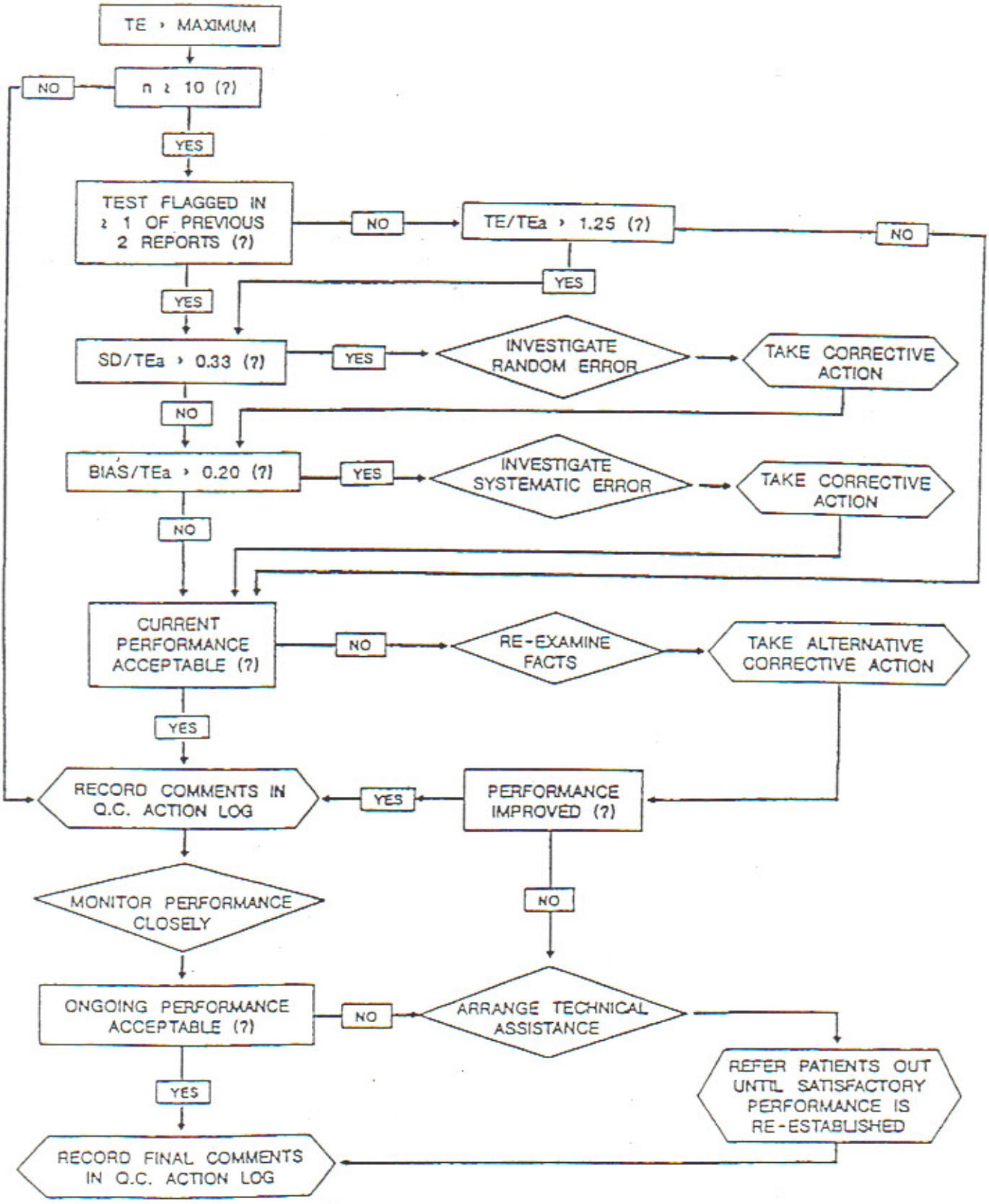
The following TEa limits indicate clinically allowable variation at observed control mean values, as set by G.R. Massarella MD, FRCP(C). These values are modified from time to time - and must be evaluated for each clinical setting.

TEST	CONTROL	SI UNITS MEAN	TEa		NON-SI UNITS MEAN	TEa	
AST (SGOT)	CH1	37.8	7.6	U/L	37.8	7.6	U/L
AST (SGOT)	CH2	141.1	28.2	U/L	141.1	28.2	U/L
Albumin	CH1	31.1	3.0	g/L	3.1	0.30	g/dL
Albumin	CH2	23.3	2.0	g/L	2.3	0.20	g/dL
Alkaline Phosphatase	CH1	56.9	11.4	U/L	56.9	11.4	U/L
Alkaline Phosphatase	CH2	274.0	54.8	U/L	274.0	54.8	U/L
Amylase	CH1	54.8	11.0	U/L	54.8	11.0	U/L
Amylase	CH2	523.3	104.7	U/L	523.3	104.7	U/L
CPK	CH1	193.3	31.4	U/L	193.3	31.4	U/L
CPK	CH2	658.6	105.8	U/L	658.6	105.8	U/L
Calcium	CH1	2.31	0.20	mmol/L	9.24	0.8	mg/dL
Calcium	CH2	3.12	0.20	mmol/L	12.50	0.8	mg/dL
Chloride	CH1	103.7	4.0	mmol/L	103.7	4.0	mEq/L
Chloride	CH2	92.5	4.0	mmol/L	92.5	4.0	mEq/L
Cholesterol	CH1	5.16	0.46	mmol/L	199.5	18.0	mg/dL
Cholesterol	CH2	4.10	0.37	mmol/L	158.6	14.3	mg/dL
Creatinine	CH1	100.7	15.0	umol/L	1.14	0.17	mg/dL
Creatinine	CH2	530.9	50.0	umol/L	6.00	0.57	mg/dL
Gamma-GT	CH1	25.7	5.1	U/L	25.7	5.1	U/L
Gamma-GT	CH2	117.6	23.5	U/L	117.6	23.5	U/L
Glucose - Fasting	CH1	4.42	0.6	mmol/L	79.6	10.8	mg/dL
Glucose - Fasting	CH2	16.04	2.0	mmol/L	288.9	36.0	mg/dL
LDH	CH1	191.1	38.2	U/L	191.1	38.2	U/L
LDH	CH2	399.3	79.9	U/L	399.3	79.9	U/L
Phosphate	CH1	1.06	0.20	mmol/L	3.28	0.62	mg/dL
Phosphate	CH2	2.68	0.40	mmol/L	8.30	1.24	mg/dL
Potassium	CH1	6.64	0.40	mmol/L	6.64	0.40	mEq/L
Potassium	CH2	3.82	0.30	mmol/L	3.82	0.30	mEq/L
Sodium	CH1	142.3	5.0	mmol/L	142.3	5.0	mEq/L
Sodium	CH2	126.2	4.0	mmol/L	126.2	4.0	mEq/L
Total Bilirubin	CH1	25.60	5.0	umol/L	1.50	0.3	mg/dL
Total Bilirubin	CH2	107.30	20.0	umol/L	6.28	1.2	mg/dL
Total Protein	CH1	66.3	6.0	g/L	6.63	0.60	g/dL
Total Protein	CH2	48.4	4.0	g/L	4.84	0.40	g/dL
Triglycerides	CH1	1.27	0.20	mmol/L	112.46	17.7	mg/dL
Triglycerides	CH2	2.21	0.40	mmol/L	195.70	35.4	mg/dL
Urate	CH1	184.3	40.0	umol/L	3.10	0.67	mg/dL
Urate	CH2	442.2	50.0	umol/L	7.43	0.84	mg/dL
Urea	CH1	5.45	1.0	mmol/L	15.27	2.8	mg/dL
Urea	CH2	18.43	2.5	mmol/L	51.62	7.0	mg/dL

AMYLASE:
PROBLEM: One lab showed mean values below other labs using the same manufacturer's reagent.
INVESTIGATION: Patient samples confirmed the bias; communication with the manufacturer indicated an incorrect reagent cal factor had been provided.
RESOLUTION: Correction of the cal factor .

URATE:
PROBLEM: A shift in mean value indicated high bias.
INVESTIGATION: The interlab SDI was high. Comparison of calibrator value to another lab revealed a discrepancy. The manufacturer's package insert was re-checked.
RESOLUTION: A revised calibrator value was entered.

TOTAL ERROR PROBLEM-SOLVING FLOW CHART



NEW LOTS

Five different patient samples spanning the analytical range and two sets of control samples were tested using the trial lot of reagent or calibrator for three to five days. Anticipated changes in bias and TE were calculated.

If the new lot's TE was < TEa, we accepted the lot and made appropriate changes in QC rule selection if indicated.

If the new lot's TE was > TEa, we performed further study and rejected the lot if indicated.

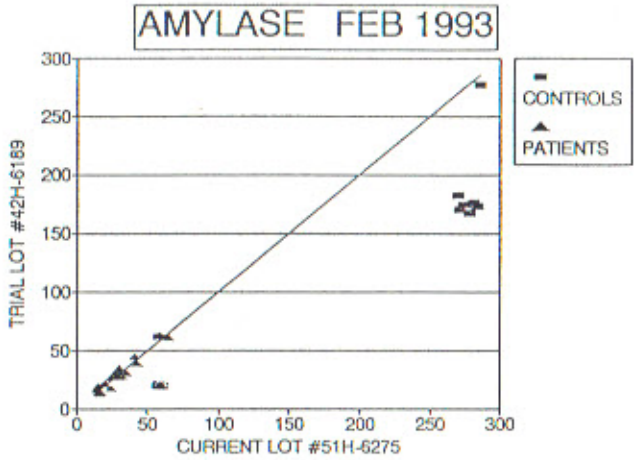
ACCEPT LOT

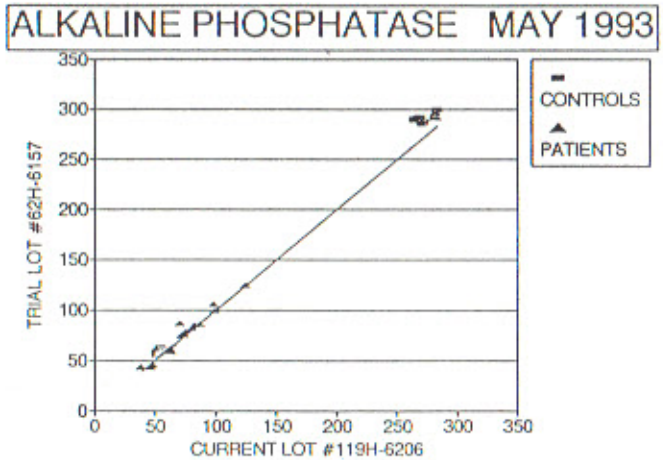
AMYLASE

Patients were unchanged; controls showed a marked shift. Pre-assessment of the lot permitted changes in QC means and avoided investigation of potential patient shift. Knowledge of the effect of the lot change on control samples explained variation in replicate proficiency samples.

ALKALINE PHOSPHATASE

Means shifted 1 SD. Results were within TEa. Pre-assessment of the lot allowed re-assignment of QC means to avoid false QC flags.





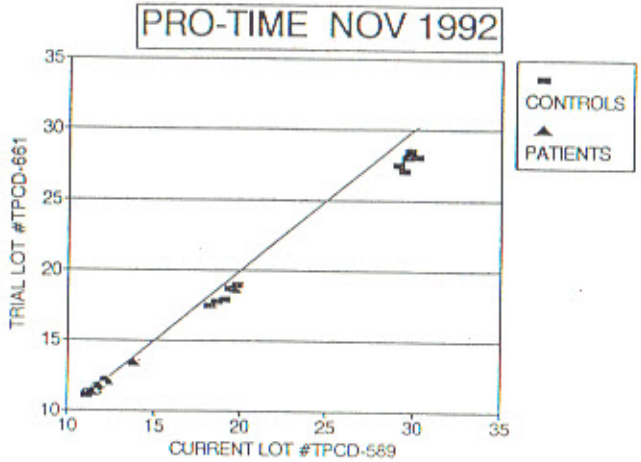
REJECT LOT

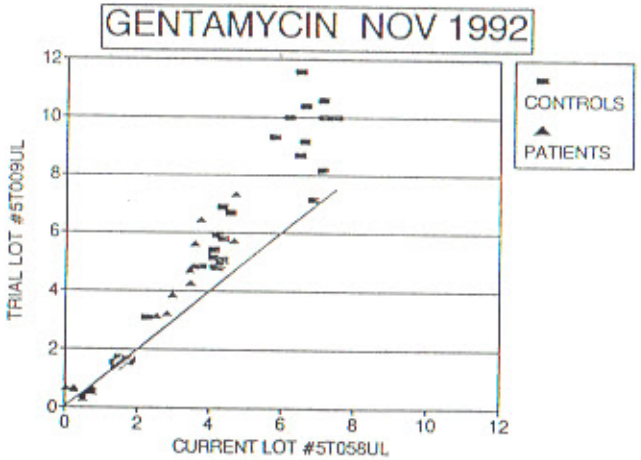
PROTHROMBIN TIME

Pre-assessment of the new lot showed a clinically unacceptable shift in control and patient values. Other labs confirmed the same shift in patient results. The manufacturer provided a replacement lot.

GENTAMYCIN

A change in reagent composition caused a shift in controls and led to clinically-different patient results. Patient samples were referred out for comparison. This method was ultimately discontinued.





QC RULES

Appropriate QC rules for 2 control samples per run are selected from Westgard's QC Selection Grids based on the stability of the method and the ^SEc in relation to TEa for each control/test.

WESTGARD QC SELECTION GRID N = 2

PROCESS CAPABILITY ΔSEc	PROCESS STABILITY (error frq'cy)		
	Poor (>10%)	Mod (2-10%)	Ex (<2%)
< 2	N/A N/A	1-2.0s N/A	1-2.5s 1-3s/2-2s/ R-4s/4-1s
2 to 3	1-2.0s N/A	1-2.5s 1-3s/2-2s/ R-4s/4-1s	1-3.0s 1-3s/2-2s/ R-4s/(4-1s)
> 3	1-2.5s 1-3s/2-2s/ R-4s/4-1s	1-3.0s 1-3s/2-2s/ R-4s/(4-1s)	1-3.5s 1-3s/(4-1s)

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WESTGARD

Determine TEa at medical decision limit

Determine Bias & SD

Calculate ^SEc [(TEa-IBiasI)/s]-1.65

Categorize stability

Choose a QCSG; Select the row based on value of ^SEc and select a column based on stability

Look up possible control rules and N

MODIFICATION

Set TEa at control means

Enter actual SD and Bias in program

Program calculates ^SEc [(TEa-IBiasI)/s]-1.65

Categorize stability

Program specifies QC rules for N=2

SAMPLE REPORT: QUALITY CONTROL RULE SELECTION

The following rule selections are based on Westgard's QC Selection Grids, using two controls per run.

TEST	STAB.	CTRL	MEAN	SD	BIAS	^SEc	SINGLE RULE	MULTI-RULE
ALB	EX	CH1	31.10	.40	-.50	4.60	1-3.5s	1-3s/(4-1sW)
ALB	EX	CH2	23.30	.30	-.40	3.68	1-3.5s	1-3s/(4-1sW)
ALP	EX	CH1	54.60	1.40	-2.30	4.84	1-3.5s	1-3s/(4-1sW)
ALP	EX	CH2	271.70	5.50	-2.30	7.90	1-3.5s	1-3s/(4-1sW)
BUN	EX	CH1	5.55	.10	.10	7.35	1-3.5s	1-3s/(4-1sW)
BUN	EX	CH2	18.25	.26	-.24	7.04	1-3.5s	1-3s/(4-1sW)
CAL	EX	CH1	2.27	.02	-.03	6.40	1-3.5s	1-3s/(4-1sW)
CAL	EX	CH2	3.08	.04	.01	2.69	1-3.0s	1-3s/2-2s/R-4s/(4-1sW)
CHO	EX	CH1	5.06	.08	-.17	2.03	1-3.0s	1-3s/2-2s/R-4s/(4-1sW)
CHO	EX	CH2	4.09	.06	-.01	4.33	1-3.5s	1-3s/(4-1sW)
CL	MOD	CH1	104.10	1.50	.40	.75	1-2.0s	WMR N/A; USE 1-2s
CL	MOD	CH2	93.10	1.00	.60	1.75	1-2.0s	WMR N/A; USE 1-2s
CPK	EX	CH1	184.80	5.80	-8.50	2.29	1-3.0s	1-3s/2-2s/R-4s/(4-1sW)
CPK	EX	CH2	635.60	9.80	-23.00	6.80	1-3.5s	1-3s/(4-1sW)
CRE	EX	CH1	98.80	3.50	-5.40	1.09	1-2.5s	1-3s/2-2s/R-4s/4-1s
CRE	EX	CH2	525.70	7.50	-25.20	1.66	1-2.5s	1-3s/2-2s/R-4s/4-1s
GLU	EX	CH1	4.37	.07	-.15	4.78	1-3.5s	1-3s/(4-1sW)
GLU	EX	CH2	16.01	.18	-.27	7.96	1-3.5s	1-3s/(4-1sW)
K	EX	CH1	6.67	.05	.03	5.75	1-3.5s	1-3s/(4-1sW)
K	EX	CH2	3.84	.05	.02	3.95	1-3.5s	1-3s/(4-1sW)
NA	EX	CH1	142.40	1.10	.10	2.80	1-3.0s	1-3s/2-2s/R-4s/(4-1sW)
NA	EX	CH2	126.50	1.00	.30	2.05	1-3.0s	1-3s/2-2s/R-4s/(4-1sW)
PHO	EX	CH1	1.06	.02	-.05	6.91	1-3.5s	1-3s/(4-1sW)
PHO	EX	CH2	2.68	.05	-.01	7.11	1-3.5s	1-3s/(4-1sW)
TBI	EX	CH1	26.30	1.00	.70	2.65	1-3.0s	1-3s/2-2s/R-4s/(4-1sW)
TBI	EX	CH2	107.90	2.30	.60	6.78	1-3.5s	1-3s/(4-1sW)
TPR	EX	CH1	66.10	1.00	-.80	3.55	1-3.5s	1-3s/(4-1sW)
TPR	EX	CH2	48.00	.70	-.40	3.49	1-3.5s	1-3s/(4-1sW)
UAC	EX	CH1	184.30	3.20	0.00	10.85	1-3.5s	1-3s/(4-1sW)
UAC	EX	CH2	443.60	5.60	6.40	6.14	1-3.5s	1-3s/(4-1sW)

EXAMPLES

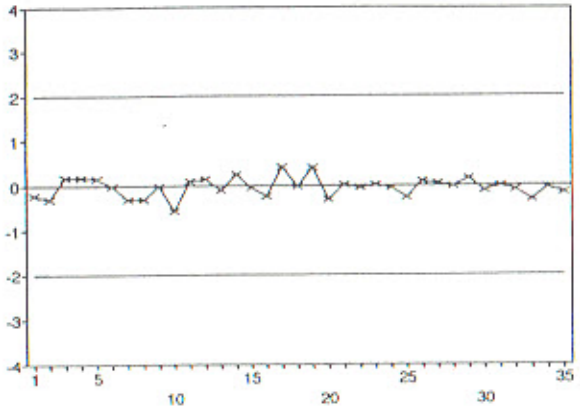
For one month's data from one lab for 24 tests, we reviewed 954 control runs. The number of runs rejected using various QC systems would have been:

Westgard Single Rule QCSG: 4
Westgard MultiRule QCSG: 23
Full Westgard Multirules: 79

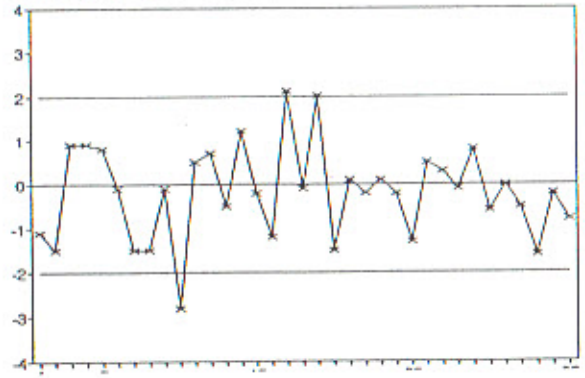
Some proficiency programs provide goals for internal QC. Setting SD limits in daily QC to match PT goals instead of using the lab's actual mean and SD fails to detect significant changes in the test system.

COMPARISON OF PROFICIENCY GOALS TO ACTUAL

CK LEVEL 2 PLOTTED vs PT TARGET

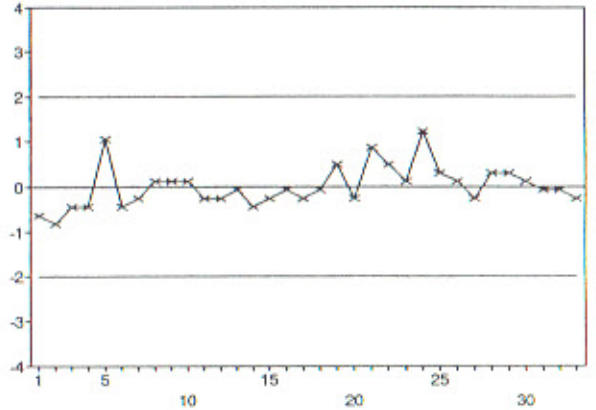


CK LEVEL 2 PLOTTED vs ACTUAL SD

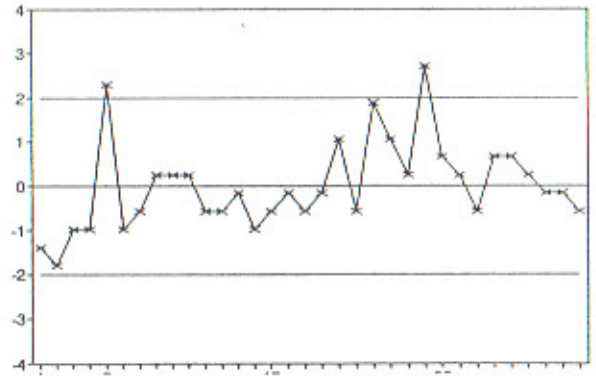


COMPARISON OF PROFICIENCY GOALS TO ACTUAL

URATE LEV 1 PLOTTED vs PT TARGET



URATE LEV 1 PLOTTED vs ACTUAL SD



CONCLUSIONS

1. Comparison of TE to TEa is a simple and effective way to monitor monthly changes in bias and imprecision.

2. Comparison of TE to TEa when changing lots of reagent or calibrator permits appropriate changes in daily QC means, identifies unacceptable lots, and provides an indication of potential changes in proficiency testing material.

3. Clinical TEa at control means can be applied to determine appropriate QC rules.