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ค่าร้อยละสัมประสิทธิ์การเปลี่ยนแปลงในการประเมินคุณภาพภายนอกระดับชาติของห้องปฏิบัติการเคมีคลินิกประเทศไทย พ.ศ. 2551-2556

สุภาวัลย์ ปิยรัตนวรสกุล และชมไฉไล สินธุสาร

สำนักมาตรฐานห้องปฏิบัติการ กรมวิทยาศาสตร์การแพทย์ ถนนติวานนท์ นนทบุรี 11000

บทคัดย่อ โครงการประเมินคุณภาพการตรวจวิเคราะห์แห่งชาติโดยองค์กรภายนอกด้านเคมีคลินิก จัดโดยสำนักมาตรฐานห้องปฏิบัติการ กรมวิทยาศาสตร์การแพทย์ กระทรวงสาธารณสุข มีวัตถุประสงค์เพื่อปรับปรุงพัฒนาและดำรงไว้ซึ่งการวิเคราะห์ที่มีคุณภาพตามมาตรฐานสากลอย่างต่อเนื่อง โครงการฯ ส่งน้ำเหลืองแห้งให้กับสมาชิกทั่วประเทศเพื่อวิเคราะห์ผล 15 รายการ จำนวน 3 รอบต่อปี รอบละ 2 ระดับ ประเมินผลการวิเคราะห์ที่รายงานผลกลับตามหลักการที่แนะนำโดยองค์การอนามัยโลก สมาชิกโครงการฯ จากปี 2551 ถึง 2556 เพิ่มจาก 841 ราย เป็น 960 ราย ผลการตรวจวิเคราะห์ของสมาชิกที่ผิดปกติอย่างชัดเจนอยู่ระหว่างร้อยละ 1.5 ถึง 3.9 ค่าคะแนนดัชนีชี้วัดคุณภาพเฉลี่ยลดลงจาก 105 เป็น 80 ค่าร้อยละสัมประสิทธิ์การเปลี่ยนแปลงที่ได้จากโครงการฯ แตกต่างจากค่าที่แนะนำโดยองค์การอนามัยโลก ระหว่าง -4.0 ถึง 2.3 และร้อยละสัมประสิทธิ์การเปลี่ยนแปลงมีค่าลดลงและคงที่ ดังนี้ sodium = 2.4, potassium = 3.5, chloride = 3.6, glucose = 5.6, cholesterol = 5.7, total protein = 6.2, albumin = 6.5, uric acid = 6.7, blood urea nitrogen = 6.9, triglycerides = 9.0, creatinine = 9.6, alanine transminase = 10.8, aspatate transminase = 11.6, total bilirubin = 15.2 และ alkaline phosphatase = 19.8 แสดงให้เห็นถึงการพัฒนาคุณภาพการตรวจวิเคราะห์ที่มีประสิทธิภาพอย่างต่อเนื่องของสมาชิกที่เข้าร่วมโครงการ

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INTRODUCTION

A medical laboratory or clinical laboratory or laboratory medicine is laboratory that provides accurate information about the health of an individual to diagnose, monitor and treat diseases, monitor patients' health and prevention of diseases.

Medical laboratory is generally divided into two sections: anatomic pathology and clinical pathology. Clinical chemistry is a section in clinical pathology that is generally concerned with analysis of components of blood urine and body fluids.

Clinical chemistry originated with the use of simple chemical tests. Subsequent to this, other techniques were applied. Most current laboratories are now highly automated to accommodate the high workload. Tests performed are closely monitored with quality controlled.

Quality control in clinical chemistry is the process that minimizes the variability of test performed, divided into two categories: Internal Quality Control (IQC) and External Quality Control (EQC). Other terms for external quality control are inter-laboratory comparisons, proficiency testing (PT) and external quality assessments schemes (EQAS).

A Thailand quality assessment in clinical chemistry program called National External Quality Assessment Scheme (NEQAS in Clinical Chemistry) was organized by the Bureau of Laboratory Quality Standards (BLQS), Department of Medical Sciences, Ministry of Public Health in 1989. The main objectives of the NEQAS are to compare test results among the participating laboratories throughout the country by using the same test items including comparisons between the test results and the ″target values″ or the ″assigned values″ in the same kind of the test items as well as to encourage the quality system establishment and implementation by laboratory personnel to take action to complete Internal Quality Control (IQC) processes. The NEQAS in Clinical Chemistry provided by BLQS was accredited the competence to comply with ISO/IEC Guide 43-1:1997(E) and ILAC G13:2000 - Guidelines for the Requirements for the Competence of Providers of Proficiency Testing Schemes on December 11, 2006 and continuously accredited the competence to comply with the requirements of ISO/IEC 17043:2010; Conformity assessment – General requirements for proficiency Testing from National Association of Testing Authorities, Australia (NATA) on June 08, 2012.

MATERIALS AND METHODS

The Bureau of Laboratory Quality Standards (BLQS) invited the government and private laboratories throughout the country to participate in the NEQAS in Clinical Chemistry. The participating laboratories will apply to the NEQAS in Clinical Chemistry so as to receive the test items, 2 bottles of lyophilized samples, same or different levels of the test substances, 3 times per year. The test items are lyophilized serum in a 5.0 mL bottle, with the shelf life of at least 1 year, to be kept at 4°C to 8°C.

The total of 15 test substances in the NEQAS in Clinical Chemistry are glucose, blood urea nitrogen (BUN), creatinine, uric acid, total cholesterol, triglyceride, total protein, albumin, total bilirubin, alanine transminase, aspatate transminase, alkaline phosphatase, sodium, potassium and chloride. These test items are carried out by BLQS to examine the homogeneity and stability test to ensure that they will not undergo any significant change throughout the conduct of the distribution.[1, 2] The participating laboratories immediately performed all substance tests within one week after receiving the test items, reconstituted the test items exactly with 5.0 mL of distilled water and placed at room temperature for at least 30 minutes, gently mixed for homogeneity. Thorough mixing was made again before testing, and then completed testing of all test substances listed within the same day of reconstitution. All tests must be performed in the routine procedures, representing the real treatment for the patient's specimens, and reporting only single results with decimal numbers of test substances. The participants converted the results to the specified units if other test units were used. Specified test procedures and equipment in the report form for test results in Clinical Chemistry scheme must be sending to the NEQAS within the closing date. If the report form is delayed for the closing date, the test results will not be evaluated.

The coordinator of the NEQAS in Clinical Chemistry will assess the results of participants to examine the performance of laboratories by using the evaluation process with correspondence with the system recommended by the World Health Organization (WHO)[3] and International Federation for Clinical Chemistry (IFCC).[4] The participants who continuously return the complete report for NEQAS in Clinical Chemistry to the Bureau of Laboratory Quality Standards within the timescale of the closing date will be given certificates. The statistical parameter composed of designated value (DV), Variance Index Score (VIS), Mean Variance Index Score (MVIS), Overall Mean Running Variance Index Score (OMRVIS) with the steps of calculation or formulas are as follows:

Designated Value (DV)

Designated Value (DV) is the mean result of the participating laboratories for that method after excluding outliers more than 3 standard deviations from the mean. The calculated steps are

1. Calculating the mean (consensus mean, $\overline{X}_1$), standard deviation (SD_1) and coefficient of variation (CV_1) from test results;
2. Omitting the test results outside ± 3 SD_1 (the outliers);
3. Recalculating the mean ($\overline{X}_2$), standard deviation (SD_2) and coefficient of variation (CV_2);
4. ($\overline{X}_2$) is used as the designated value (DV) for calculation of variance index scores.

Variance Index Score (VIS)

Variance Index Score (VIS) is positive (no negative value) and shows comparisons of results in each test, and has the value ranging from 0-400. The formula of VIS value is

$$VIS = \frac{X - DV}{DV} \times \frac{10,000}{CCV}$$

..... Formula I

X stands for test results from participants.

Chosen Coefficient of Variation (CCV)[5] is shown in Table 1.

Table 1 Chosen coefficients of variation used for calculation of VIS of individual tests

Test substances	CCV	Test substances	CCV
Glucose	7.7	Blood Urea Nitrogen (BUN)	5.7
Creatinine	8.9	Uric acid	7.7
Total protein	3.9	Albumin	7.5
Total bilirubin	19.2	Aspartate transaminase (AST)	**10.0***
Alanine transaminase (ALT)	**10.0***	Alkaline phosphatase (ALP)	**10.0***
Total cholesterol	7.6	Triglyceride	**10.0***
Sodium	1.6	Potassium	2.9
Chloride	**10.0***		

*Obtained value from the determinations during the first two years of the scheme

Mean Variance Index Score (MVIS)

Mean Variance Index Score (MVIS) has the value ranging from 0 to 400. MVIS value is positive (no negative value) and shows overall comparisons of test results from each test item or each trial. The calculated formula of Variance Index Score (VIS) is

$$VIS = \frac{X - DV}{DV} \times \frac{10,000}{CCV}$$

.....Formula II

Overall Mean Running Variance Index Score (OMRVIS)

Overall Mean Running Variance Index Score (OMRVIS) has the value ranging from 0–400 OMRVIS value is the mean of latest 30 VIS values in continuous backward sequence, positive (no negative value) and shows overall continuous comparisons of quality of each test item or each trial, is calculated from the formula:

$$OMVIS = \frac{\Sigma\ VIS_{30}}{30}$$

.....Formula III

Acceptable scores for the quality standard performance

The acceptable scores for the quality standard performance for VIS, MVIS of each test and OMRVIS (overall performance) of the participants are equal to or less than 150.

RESULTS

At present to date, the NEQAS in Clinical Chemistry has continuously performed 148 trials for proficiency test of 15 general chemistry tests, 2 trials per cycle and 3 cycles per year.

The NEQAS in Clinical Chemistry has provided applications to the clinical chemistry laboratories in the country. The number of participants was 841 laboratories in 2008 and 960 laboratories in 2013. They were divided by general hospitals and community health hospitals, private hospitals including polyclinics, and others from university hospitals, military hospitals, state enterprise service hospitals, and bangkok metropolitan hospitals as shown the percent distribution of participants (Table 2).

Table 2 The percent of participant laboratories distribution throughout the country, applied to the NEQAS in Clinical Chemistry from year 2008 to 2013

↓ Participating Laboratories — Year →	2008	2009	2010	2011	2012	2013	Total
general hospitals and community health hospitals	73.01	71.93	72.04	73.32	71.88	70.00	72.03
private hospitals and polyclinics	21.28	22.97	22.04	20.42	22.58	23.54	22.14
university hospitals	2.50	1.74	1.90	2.20	1.95	2.08	2.06
military hospitals	2.38	2.55	3.20	3.25	2.82	3.54	2.96
state enterprise service hospitals, and bangkok metropolitan hospitals	0.83	0.81	0.83	0.81	0.76	0.83	0.81
Total	100.00	100.00	100.00	100.00	100.00	100.00	100.00

The average MVIS of participating laboratories decreased from the value of 105 to 80 as (Figure 1). About 16% of participants indicated the very good quality results. It was found that the MVIS 0-50 and 50% of participants indicated the good quality MVIS 51-100 while 24% of participants were at medium quality results. It was found that the MVIS 101-150 and 10% of participants were unacceptable quality results, MVIS more than 151 (Table 3).

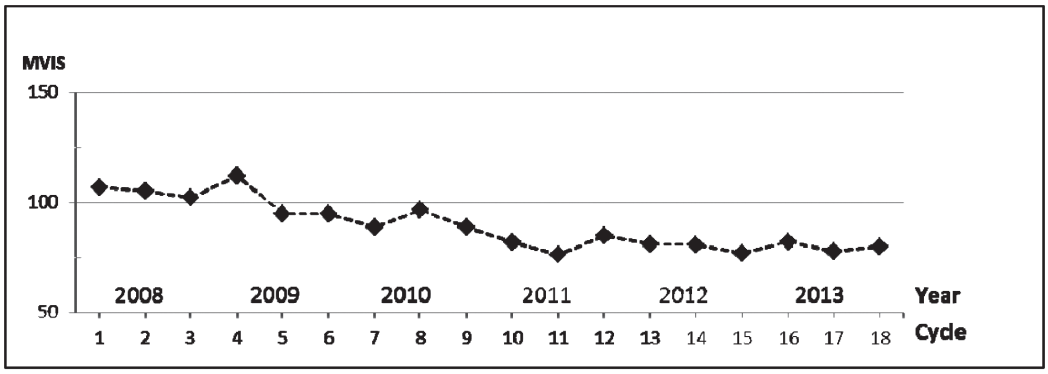

Figure 1 MVIS of 15 general chemistry tests from participants Thailand NEQAS in Clinical Chemistry: 2008–2013

Table 3 Percent (average) of the laboratories according to MVIS level of Thailand NEQAS in Clinical Chemistry: 2008–2013

↓ MVIS level	Years →	Percent (average) of the laboratories						
		2008	2009	2010	2011	2012	2013	average
0–50		8.3	8.8	11.2	24.4	22.1	21.6	16.1
51–100		44.7	48.5	52.6	46.3	54.7	55.2	50.3
101–150		31.7	29.4	25.6	19.2	17.8	18.1	23.6
151–200		10.3	9.4	7.7	8.5	4.2	3.8	7.3
201–250		3.0	2.8	2.2	0.7	0.8	0.8	1.7
251–300		1.0	0.9	0.4	0.2	0.2	0.4	0.5
301–350		1.0	0.1	0.2	0.1	0.2	0.1	0.3
351–400		0.0	0.1	0.1	0.5	0.0	0.1	0.2

The evaluation system used in this scheme is the system recommended by the World Health Organization and International Federation for Clinical Chemistry. The first step is the omitting of the outliers (mean ± 3 SD) then to calculate the Designated Value (DV). The percent outliers (average) of 15 test substances which were omitted from the participants range from 1.5% to 3.9% (Table 4).

Figure 2 shows the percent CV of 15 analyses from participants Thailand NEQAS in Clinical Chemistry from the year 2008 to 2013. It is clearly shown that the % CV during the last three years (2011 to 2013) from the results of the scheme was consistently continuous, except the results of aspatate transminase slightly upward trend in the last year (2013).

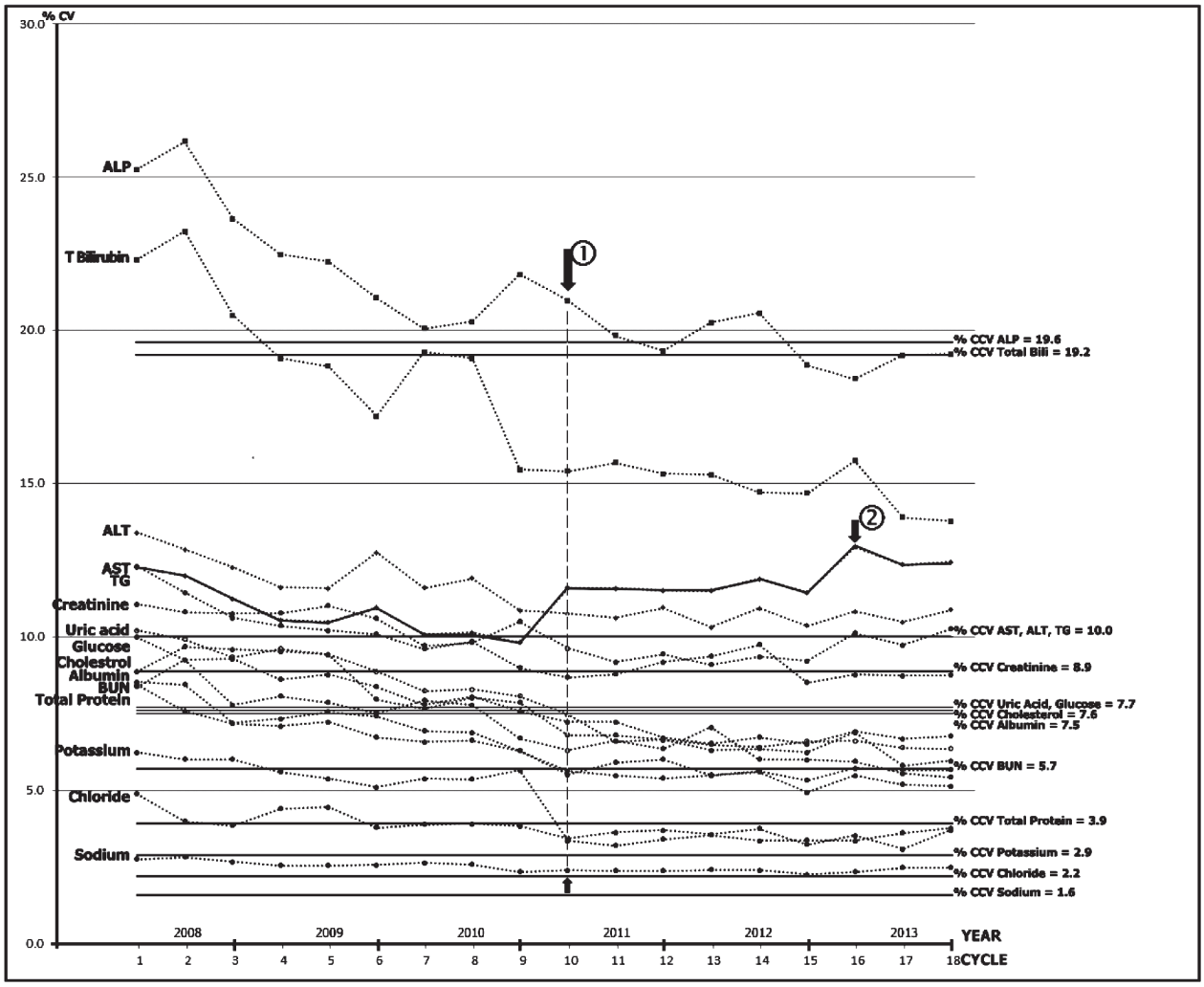

Figure 2 Percent CV of 15 general chemistry tests from participants Thailand NEQAS in Clinical Chemistry: 2008–2013

Table 4 Percent outliers (average) of 15 test substances reported by participants of Thailand NEQAS in Clinical Chemistry: 2008-2013

Test substances	Number of result and % Outliers	2008	2009	2010	2011	2012	2013
Glucose	Number of result	725	737	752	787	817	839
	%Outliers	2.7	2.7	3.0	2.7	2.6	2.4
BUN	Number of result	774	777	784	813	840	856
	%Outliers	3.2	2.7	3.3	2.7	2.8	2.5
Creatinine	Number of result	772	781	784	814	840	855
	%Outliers	2.3	2.2	2.0	2.4	2.3	2.0
Uric Acid	Number of result	765	772	775	807	834	850
	%Outliers	3.3	2.9	2.7	3.6	3.2	3.6
Total Protein	Number of result	720	723	730	762	793	811
	%Outliers	2.8	2.4	2.7	3.0	2.3	3.5
Albumin	Number of result	722	729	736	769	796	814
	%Outliers	2.6	2.2	2.6	3.3	3.4	3.4
Total Bilirubin	Number of result	722	728	736	765	791	808
	%Outliers	3.3	3.6	2.4	3.4	2.5	2.9
Aspartate	Number of result	763	771	779	808	838	850
transaminase	%Outliers	3.4	2.9	3.2	2.9	1.9	1.7
Alanine	Number of result	763	772	779	808	836	850
transaminase	%Outliers	3.3	2.6	2.9	3.0	2.6	2.9
Alkaline	Number of result	747	759	767	800	828	841
phosphatase	%Outliers	1.9	2.2	1.8	1.9	2.7	2.9
Cholesterol	Number of result	756	753	771	811	838	852
	%Outliers	3.0	2.8	2.9	2.9	2.5	2.6
Triglyceride	Number of result	757	772	773	809	836	848
	%Outliers	2.6	3.0	2.4	3.2	2.5	2.7
Sodium	Number of result	594	624	664	717	746	762
	%Outliers	2.8	2.9	2.5	2.5	2.3	1.8
Potassium	Number of result	625	644	672	723	754	767
	%Outliers	3.9	3.0	2.7	2.1	1.6	1.5
Chloride	Number of result	597	624	664	714	745	761
	%Outliers	1.5	2.0	2.3	2.5	2.1	1.9

The NEQAS in Clinical Chemistry reported the new %CCV from the determinations during the last three years of the scheme, 2011-2013 except the results of aspatate transminase (AST) from 2011-2012 as shown in Table 5. The difference of the %CV (average) calculated from 15 test substances of the participants from the %CCV recommended by WHO range from -4.0 (the %CV of total bilirubin is less than the %CCV: 19.2-15.2) to 2.3 (the %CV of total protein is more than the %CCV: 6.2-3.9). The percent CV from NEQAS of Clinical Chemistry Laboratory in Thailand are significant difference (95% Confidence Interval) from the %CCV recommended by WHO, accept alkaline phophatase (ALP).

Table 5 New %CCV from the determination during the last three years of the scheme, 2011-2013 except Aspartate transaminase from 2011-2012

Test substances	% CV NEQAS	% CCV WHO	Difference	P value	95% Confidence Interval of the Difference	
					Lower	Upper
Total Bilirubin	15.2	19.2	-4.0**	.000	-4.73	-3.31
Glucose	5.6	7.7	-2.1**	.000	-2.46	-1.84
Cholesterol	5.7	7.6	-1.9**	.000	-2.18	-1.72
Triglyceride	9.0	10.0*	-1.0**	.000	-1.28	-0.66
Albumin	6.5	7.5	-1.0**	.000	-1.33	-.59
Uric Acid	6.7	7.7	-1.0**	.000	-1.31	-5.7
ALP	19.8	19.6	0.2	.555	-.48	.84
Potassium(K)	3.5	2.9	0.6**	.000	.47	.80
Creatinine	9.6	8.9	0.7**	.001	.40	1.02
ALT	10.8	10.0*	0.8**	.000	.53	1.00
Sodium (Na)	2.4	1.6	0.8**	.000	.78	.87
BUN	6.9	5.7	1.2**	.000	.92	1.46
Chloride(Cl)	3.6	2.2	1.4**	.000	1.10	1.62
AST	11.6	10.0*	1.9**	.000	1.40	1.77
Total Protein	6.2	3.9	2.3**	.000	1.934	2.727

* Obtained value from the determinations during the first two years of the scheme

** Significant difference (95% Confidence Interval)

DISCUSSION

The NEQAS in Clinical Chemistry is the large external quality control scheme, where the submitted results grouped by the principle of analysis were at least 100 participants. The percent of overall trimming ranging from 1.5% to 3.9% shown in Table 4 were less than 10% which can be used routinely (6). The performance of different laboratories is assessed by the statistical parameters that calculated using these trimmed results; it is clear that such an index will not be distorted by any outlying value.

The variance index score (VIS) shows comparisons of results in each test and has the value ranging from 0-400, calculated using formular I through the chosen coefficient of variation (CCV) shown in Table 1, accepted the CCV of aspatate transminase, alanine transminase, alkaline phosphatase, triglyceride and chloride which were obtained during the first two years of the NEQAS.

The improvement in the performance of laboratories can be detected by the average MVIS of participating laboratories deceased from the value of 105 to 80 as shown in Figure 1. About 16% of participants had very good quality MVIS of 0-50 and 50% at good quality MVIS of 51-100 as shown in Table 3.

The NEQAS in Clinical Chemistry reported the new %CCV from the determinations during the last three years of the scheme, 2011-2013 except aspatate transminase that from 2011-2012 as shown in Table 5.

The difference of the %CV (average) of 15 test substances of the participants from the %CCV recommended by WHO, range from -4.0 (the %CV of total bilirubin is less than the %CCV: 19.2-15.2) to 2.3 (the %CV of total protein is more than the %CCV: 6.2-3.9).

CONCLUSION

The NEQAS in Clinical Chemistry reported the new percent coefficient of variation of sodium = 2.4, potassium = 3.5, chloride = 3.6, glucose = 5.6, cholesterol = 5.7, total protein = 6.2, albumin = 6.5, uric acid = 6.7, BUN = 6.9, triglyceride = 9.0, creatinine = 9.6, alanine transminase = 10.8, aspatate transminase = 11.6, total bilirubin = 15.2 and alkaline phosphatase = 19.8. The %CV of 15 tests obtained during the last three years were constantly kept, showing the performance improvement of participating laboratories of Thailand NEQAS in clinical chemistry.

The NEQAS in Clinical Chemistry, Bureau of Laboratory Quality Standards, Department of Medical Sciences, Ministry of Public Health managed the proficiency test from ISO/IEC Guide 43-1:1997 and was accredited for the facility complied with ILAC G13:2000 - Guidelines for the Requirements for the Competence of Providers of Proficiency Testing Schemes on December 11, 2006 and accredited the facility complied with the requirements of ISO/IEC 17043:2010 Conformity assessment - General requirements for proficiency testing from National Association of Testing Authorities, Australia (NATA) on June 08, 2012.

The main objectives are not only to compare test results among the participating laboratories throughout the country but also to encourage the quality system establishment and implementation by laboratory personnel to take action to complete of Internal Quality Control (IQC) processes, as well as to boost up laboratory services to improve and maintain sustainable quality monitoring leading to the international standards.

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The Percent CCV From National External Quality Assessment of Clinical Chemistry Laboratory in Thailand, 2008-2013 Experience

Supawan Piyaratanavarasakul and Chomchilai Sinthusarn

Bureau of Laboratory Quality Standards, Department of Medical Sciences, Tiwanond Road, Nonthaburi 11000, Thailand.

ABSTRACT A Thailand National External Quality Assessment scheme (NEQAS) in Clinical Chemistry was organized by the Bureau of Laboratory Quality Standards, Department of Medical Sciences, Ministry of Public Health. The objectives were to improve and maintain the sustainable quality monitoring leading to the international standards. The test items: 2 lyophilized samples were distributed to the participants throughout the country, 3 cycles per year. The returned reports from participants were grouped by the principle of analysis and evaluated by the system as recommended by the World Health Organization. In 2013, the NEQAS continuously performed 148 trials for 15 general chemistry tests from 960 laboratories throughout the country. From the year 2008 to 2013, the outlier results that were omitted range from 1.5% to 3.9% of participant results. The average MVIS of participating laboratories decreased from 105 to 80. The %CV of the participants and the %CCV recommended by WHO, differed from -4.0 to 2.3. The NEQAS reported the % CV of sodium = 2.4, potassium = 3.5, chloride = 3.6, glucose = 5.6, cholesterol = 5.7, total protein = 6.2, albumin = 6.5, uric acid = 6.7, blood urea nitrogen = 6.9, triglyceride = 9.0, creatinine = 9.6, alanine transminase = 10.8, aspatate transminase = 11.6, total bilirubin = 15.2 and alkaline phosphatase = 19.8. Furthermore, the %CV of 15 tests obtained during the last three years were found consistent thus indicating the improvement of participating laboratories and maintenance of the sustainable quality in clinical chemistry.

Keywords: NEQAS, National External Quality Assessment scheme, laboratory, %CCV, percent chosen coefficient of variation, clinical chemistry