

# The Gold-Standard Multi-Center for Hematology Laboratory Standardization in Thailand (GSMC-Thailand): A Model of National and International Integration Program (Year 2003)

Ahnond BUNYARATVEJ<sup>\*1</sup>, Prasit CHANARAT<sup>\*2</sup>, Montein PUNTUMETAKUL<sup>\*3</sup>, Jittawat RUNGJEADPHA<sup>\*4</sup>, Siripak PHANYAPORNUSUK<sup>\*5</sup>, Pornthip LEAMMUKDA<sup>\*5</sup>, Atsushi SHIRAKAMI<sup>\*6</sup>, Katsuya WADA<sup>\*6</sup>, and Keiji FUJIMOTO<sup>\*6</sup>

<sup>\*1</sup> Department of Pathology, Faculty of Medicine, Ramathibodi Hospital, Bangkok 10400, Thailand.  
Blood Disease Diagnosis Center, Sirikit Medical Center

Institute of Science and Technology for Research and Development, Mahidol University, Thailand.

<sup>\*2</sup> Department of Clinical Microscopy, Faculty of Associated Medical Sciences, Chiang Mai University, 50200 Thailand.

<sup>\*3</sup> Department of Clinical Microscopy, Faculty of Associated Medical Sciences, Khon Kaen University, 40002, Thailand.

<sup>\*4</sup> Department of Pathology, Faculty of Medicine, Prince of Songkla University, 40002, Thailand.

<sup>\*5</sup> Meditop Co., Ltd, 10310, Thailand.

<sup>\*6</sup> Sysmex Corporation, 4-4-4 Takatsukadai, Nishi-ku, kobe 651-2271, Japan.

Over 62 million people distributed in 4 geographical regions, central, north, north-eastern, and southern regions in Thailand. Thai people have their right to equally receive good medical care under the health insurance from government. Hematology laboratories, over 2,000 sites including governmental and private sectors in this country, have to take responsibilities for providing hematology data. A wide range of technology, methods and standard criteria have been implemented among these laboratories. Harmonization of the hematology laboratories with standard service all over the country is the major goal to reach. In 1998, an attempt to share experience of laboratory proficiency has been done under the name of Golden-Standard or Gold-Standard External Quality Assurance (EQA) program. This is the collaborating effort between Scientific Division, Sysmex Corporation and Clinical Laboratory Standardization Center Blood Disease Diagnosis Center, Ramathibodi hospital, Mahidol University. The activities have been gradually and continuously progressive since then until the present time. More task forces have joined the activities, including governmental sectors: Prince of Songkla University, Khon Kaen University, Chiang Mai University and private sector Meditop Thailand. All of these task forces have become to be EQA center in each geographical region, of four years have passed, each center become strengthen with more and more participating people and organization. We report our 5-year experience of multi-center for gold-standard program as the national projects covering increasing numbers of nation-wide laboratory members. The Gold-Standard Multi-Center program is a good example model of integration among various institutes both governmental and private sectors and international collaboration.

(Sysmex J Int 13 : 90-96, 2003)

## Key Words

External Quality Assurance, Hematology Analyzer, Hematology Standardization, Laboratory Network

Received 26 November, 2003, Accepted 2 December, 2003

## INTRODUCTION

The golden-standard project has been triggered five years ago. The Clinical Laboratory Standardization Center (CLSC) was established by Professor Ahnond Bunyaratvej under the support of Scientific Division of Sysmex Corporation (Kobe, Japan) managed by Mr. Keiji Fujimoto. The activity of CLSC was firstly initiated in Bangkok, and Salaya Nakorn Pathom, Mahidol University. The concept of multi-center program in Thailand was proposed for two reasons: one was the different geographic location and the other was the discrepancy of hematological abnormalities found in different regions in Thailand. For example, malaria cases in the central part

and neighboring area, high incidence of hemoglobin E in northeastern, ovalocytosis and spherocytosis in the south and higher incidence of  $\alpha$ -thalassemia in the north. However, the priority of normal sample handling must come first because there have been a wide range of technology among hematology laboratories in Thailand. Then, at the beginning, the main duty of gold-standard program was concentrating on installation of the gold-standard blood cell analyzers in various centers and on-site exchanged expertise. The expertise from 1 center has been exchanged with another center, year by year. Ramathibodi hospital, Mahidol University was the 1<sup>st</sup> place of gold-standard blood cell analyzer installation in

August, 1998<sup>1)</sup>, then Prince of Songkla University (PSU) in December, 2000, Khon Kaen University (KKU) in June, 2000 and Chiang Mai University (CMU) in October, 2001. External Quality Assurance (EQA) has been carried out since 1998 until now 7 phases. The 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> EQA were performed in August 1998, May 1999 and December 1999 respectively by a single center, CLSC at BDDC (Blood Disease Diagnosis Center, Sirikit Medical Center, Ramathibodi Hospital, Mahidol University, Thailand). The CLSC had further extension within Mahidol University to Institute of Science and Technology for Research and Development, at Golden Standard Unit of Cell Engineering and Tissue Growth (CETG) research laboratory in Salaya, Mahidol University. The CETG has been installed both golden-standard in 1998 and reference standard machines in 1999. The reference standard machine and all 4 gold-standard machines of all 4 regions have been calibrated and run the EIGHTCHECK-3WP (Streck Laboratories, Inc., USA) control every day. All these continuous efforts have been done by representatives which are now becoming the EQA program under the continuous support from Scientific Division of Sysmex Corporation. 4-year experience has shown that the activities and movement of multi-center gold standard program are totally non-profit activities. No commercialization and no member fee from participating laboratory members. All movements are for the academic and scientific merit. Now, the centers of EQA have been set up in all parts of Thailand. Each center has performed EQA activity with laboratory members. The annual meeting of representative members from all multi-centers so-called Gold-Standard Multi-Center Meeting (GSMC Meeting) was set up during October 13-14, 2003. This is the second GSMC Meeting after the 1<sup>st</sup> one in Song Khla. The conclusion from the meeting is to publish our activities to international publication. Sysmex Journal International is our choice since readers and subscribers are in this field.

## MATERIALS AND METHODS

We run EQA program in harmonization among multicenters in 4 geographical regions in Thailand. 7 phases of EQA studies have been performed with our participating laboratory members.

### Materials

In each survey, Hematology Control Material, the EIGHTCHECK-3WP was distributed to participant laboratories, summarized in *Table 1*.

### Distribution

From 1<sup>st</sup> to 3<sup>rd</sup> survey, samples were distributed nationwide without coolant by EMS from CLSC, Bangkok. After the 4<sup>th</sup> survey, the local center hospitals were responsible for distributing the samples to their covered regions, such as the south part for PSU, the north east part for KKU and the north part for CMU.

### Data analysis

All participant laboratories were divided into statistical peer groups based on the manufacturer and method. Results for each participant were evaluated and expressed according to the peer group mean and standard deviation index (SDI) methods. The peer group mean was derived from the group mean after removing outliers detected by double-truncation with +/- 3SD. The SDI was determined using the following calculation:

$$SDI = (\text{participant data} - \text{peer group mean}) / \text{peer group SD}$$

## RESULTS

### Participant laboratories

*Fig. 1* shows the historical change on number of participant laboratories from 1<sup>st</sup> to 7<sup>th</sup> survey. Total numbers of participants have increased from 210 to 348 laboratories in these 4 years.

### Summarized results of 7<sup>th</sup> EQA

*Fig. 2* shows the status of internal QC performance at each laboratory. Except for Group 8 (manual method), 97.5% of participants in this survey performed internal QC using control materials. As for manual method, only 2 laboratories of 21 laboratories do the internal QC.

*Tables 2-6* show the summarized results of peer group data of the 7<sup>th</sup> survey for WBC, RBC, HGB, HCT and PLT, after removing outliers detected by double-truncation with +/- 3SD.

### Historical change of inter-laboratory CV

*Figs. 3-7* show the historical change of Inter-laboratory CV(%) from 1<sup>st</sup> to 7<sup>th</sup> survey for WBC, RBC, HGB, HCT and PLT, after removing outliers detected by double-truncation with +/- 3SD.

Except for manual method group, inter-laboratory CV for each peer group has been gradually improving for WBC, HGB and PLT. Especially for HGB, the inter-laboratory CV of all peer groups except for manual method was under 4%.

## DISCUSSION AND MULTI-CENTER REPORTS

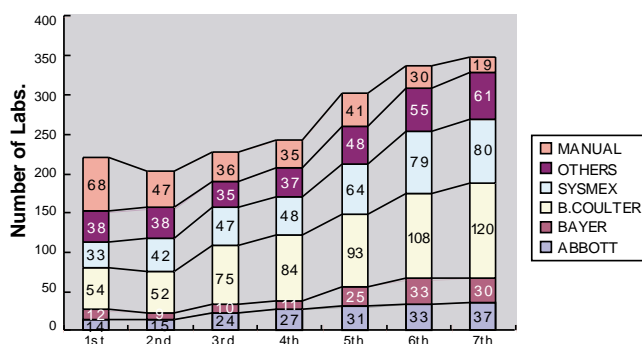
### The EQA centers from all regions have summarized activities

#### Central region

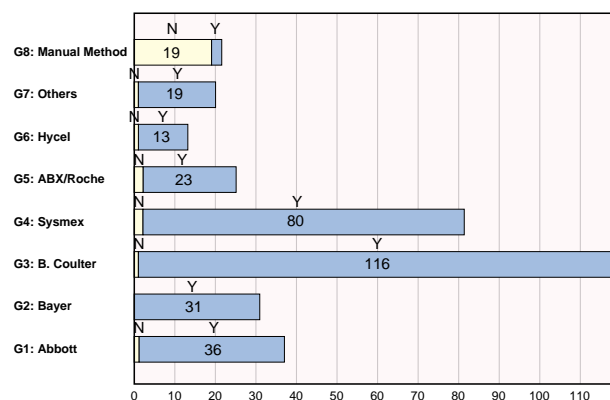
Since 1998, Scientific Division of Sysmex Corporation has been supporting the EQA activities in Thailand, which Professor Ahnond Bunyaratvej, director of CLSC, Ramathibodi Hospital, Mahidol University organized under collaboration with the Ministry of Public Health<sup>2,3)</sup>. In these 4 years, the "nation-wide" Hematology EQA was executed 7 times. The number of participant laboratories has been gradually increasing – 210 (1<sup>st</sup>), 209 (2<sup>nd</sup>),

**Table 1** Summary of 1<sup>st</sup> - 7<sup>th</sup> EQA programs

When	1 <sup>st</sup> EQA '98-Aug	2 <sup>nd</sup> EQA '99-May	3 <sup>rd</sup> EQA '99-Dec	4 <sup>th</sup> EQA '00-Jun	5 <sup>th</sup> EQA '00-Dec	6 <sup>th</sup> EQA '01-Oct	7 <sup>th</sup> EQA '02-NOV
Participants #	210	209	227	242	302	336	348
EQA sample (Level)	Eightcheck-C (Normal)	Eightcheck-C (Normal)	Eightcheck-C (Normal)	Eightcheck-C (Normal)	Eightcheck-C (Low)	Eightcheck-C (High)	Eightcheck-C (Low)
Performed by	CLSC	CLSC	CLSC	CLSC +PSU	CLSC +PSU +KKU	CLSC +PSU +KKU +CMU	CLSC +PSU +KKU +CMU



**Fig. 1** Historical change on number of participants



**Fig. 2** Internal QC status (from 7<sup>th</sup> survey)

227 (3<sup>rd</sup>), 242 (4<sup>th</sup>), 302 (5<sup>th</sup>), 336 (6<sup>th</sup>) and 348 (7<sup>th</sup>). From the 4<sup>th</sup> EQA performed in June, 2000, the multi-center laboratories system has been introduced to improve the sample-distribution and the follow-up processes – the 3 local-center hospital joined, PSU and KKU in 2000 and CMU in 2001.

EQA schemes are now performed widely at national, regional levels or worldwide, and many laboratories concern their results or performance. The EQA has started since 1998. There are 87 hospitals participating the EQA. The participants were categorized into 6 groups based on manufacturer of the hematology analyzer such as 1) Abbott, 2) Bayer, 3) Beckman-Coulter, 4) Sysmex, 5) others and 6) manual method. But in the latest EQA phase we could categorize to 8 statistic groups as

1) Abbott, 2) Bayer, 3) Beckman-Coulter, 4) Sysmex, 5) ABX and Roche, 6) Hycel, 7) others and 8) manual method. Automated machines using in Thailand have shown to have different CV among various company. We found that the CV values of HGB, HCT and RBC were acceptable (less than 7) in all groups of different companies. However, the CV values of WBC and PLT were relatively high. This may result from calibration system is variable among various companies. However, we should consider that some groups have relatively low number of participants. Quality management is also one main important issue to be trained in the laboratory<sup>4)</sup>.

In conclusion, this study has shown condition of hematology laboratories in Thailand that considerable numbers of participants (31.1%) have used manual counting.

Although the rest of participants have automated machines, WBC and PLT are to be closely monitored. Further finding of PLT methods may be applied to solve this problem<sup>5)</sup>. The red cell parameters have satisfactory CV indicating good management in calibration. This also indicates that climate and geography of Thailand are not an obstacle in performing EQA program.

### Northern region

Department of Clinical Microscopy (CMS), Faculty of Associated Medical Sciences (AMS), Chiang Mai University (CMU) has started the EQA Program in Thailand since 2001. The department had launched the 7<sup>th</sup> EQA in since November 2002 on the 2<sup>nd</sup> year of participation. The program has been launched once a year since 1996 with a co-operation between Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University in Bangkok, Thailand and Sysmex Corporation<sup>3, 5)</sup>. In order to set up a tool for hematology laboratory accreditation, which required many means of standard method. All 76 participants were sent the analysis data back to the CMU site. These consisted of 7 university hospitals, 9 tertiary or specialized hospitals, 16 general hospitals, 9 community hospitals, 21 private hospitals and 6 military or other hospital laboratories. The stability checkup during the process fell within the acceptable range. In overall data, the performance was excellent over 70% (within  $\pm 1SD$ ), good ~20% (within  $\pm 2SD$ ), fair ~7% (within  $\pm 3SD$ ) and poor for only <1.5%

**Table 2** 7<sup>th</sup> EQA results for WBC

(Unit: ×10<sup>3</sup>/μL)

Peer Group	n	Mean	SD	CV(%)	MIN	MAX
G1: Abbott	36	2.49	0.32	13.05	1.75	3.38
G2: Bayer	30	2.50	0.11	4.32	2.24	2.74
G3: Beckman-Coulter	119	2.62	0.12	4.67	2.32	2.92
G4: Sysmex	78	2.43	0.09	3.79	2.26	2.68
G5: ABX/Roche	26	2.45	0.12	4.71	2.20	2.64
G6: Hycel/DANAM	15	2.58	0.13	5.07	2.38	2.86
G7: Others	19	2.60	0.21	7.98	2.13	2.96
G8: Manual Method	19	2.26	0.44	19.65	1.46	2.86

**Table 3** 7<sup>th</sup> EQA results for RBC

(Unit: ×10<sup>6</sup>/μL)

Peer Group	n	Mean	SD	CV(%)	MIN	MAX
G1: Abbott	37	2.48	0.08	3.40	2.29	2.73
G2: Bayer	30	2.42	0.13	5.26	2.09	2.76
G3: Beckman-Coulter	120	2.41	0.05	2.23	2.25	2.53
G4: Sysmex	78	2.41	0.05	2.21	2.27	2.57
G5: ABX/Roche	26	2.40	0.07	3.09	2.18	2.55
G6: Hycel/DANAM	15	2.45	0.10	4.14	2.29	2.60
G7: Others	19	2.44	0.11	4.50	2.27	2.76
G8: Manual Method	2	2.41	0.15	6.18	2.31	2.52

**Table 4** 7<sup>th</sup> EQA results for HGB

(Unit: g/dL)

Peer Group	n	Mean	SD	CV(%)	MIN	MAX
G1: Abbott	37	6.81	0.29	4.24	6.06	7.64
G2: Bayer	29	6.73	0.14	2.07	6.50	7.08
G3: Beckman-Coulter	116	6.62	0.14	2.07	6.20	6.90
G4: Sysmex	78	6.66	0.09	1.41	6.42	6.86
G5: ABX/Roche	25	6.61	0.15	2.31	6.22	6.98
G6: Hycel/DANAM	15	6.72	0.25	3.68	6.02	7.04
G7: Others	19	6.69	0.27	4.08	6.32	7.20
G8: Manual Method	3	6.63	0.75	11.36	5.76	7.12

**Table 5** 7<sup>th</sup> EQA results for HCT

(Unit: %)

Peer Group	n	Mean	SD	CV(%)	MIN	MAX
G1: Abbott	37	18.92	1.05	5.54	16.68	20.88
G2: Bayer	30	17.43	1.24	7.14	15.06	20.96
G3: Beckman-Coulter	117	18.36	0.45	2.45	17.36	19.60
G4: Sysmex	78	17.73	0.64	3.64	16.00	19.66
G5: ABX/Roche	25	18.15	0.65	3.60	16.74	19.22
G6: Hycel/DANAM	15	19.05	1.13	5.96	17.00	21.30
G7: Others	19	19.09	0.58	3.06	18.14	20.22
G8: Manual Method	19	18.47	3.28	17.78	15.60	27.60

**Table 6** 7<sup>th</sup> EQA results for PLT

(Unit: ×10<sup>3</sup>/μL)

Peer Group	n	Mean	SD	CV(%)	MIN	MAX
G1: Abbott	36	59.66	4.15	6.96	50.8	69.8
G2: Bayer	29	59.78	6.41	10.73	46.0	71.8
G3: Beckman-Coulter	116	53.63	3.24	6.03	47.0	61.6
G4: Sysmex	76	54.74	4.33	7.92	46.8	65.4
G5: ABX/Roche	26	57.99	7.09	12.22	44.6	73.6
G6: Hycel/DANAM	15	63.23	7.59	12.00	51.0	77.8
G7: Others	19	62.06	9.89	15.94	46.4	84.6
G8: Manual Method	7	68.56	14.58	21.26	50.4	94.0

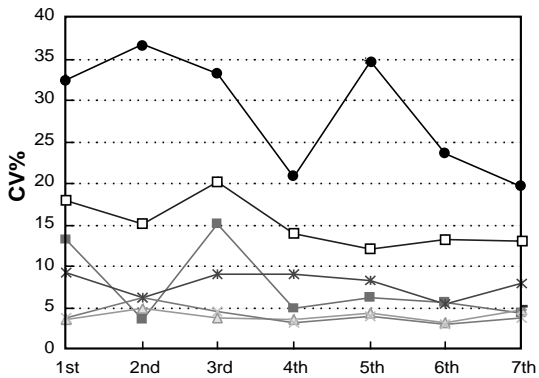


Fig. 3 Historical change of inter-laboratory CV for WBC

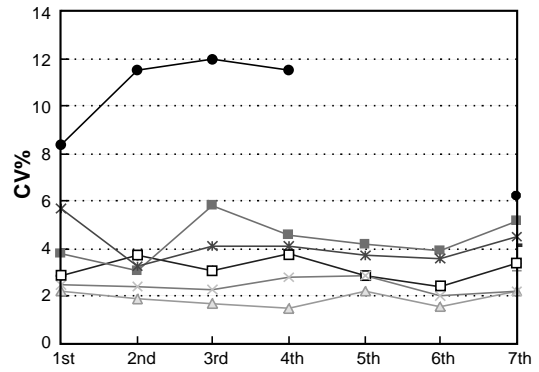


Fig. 4 Historical change of inter-laboratory CV for RBC

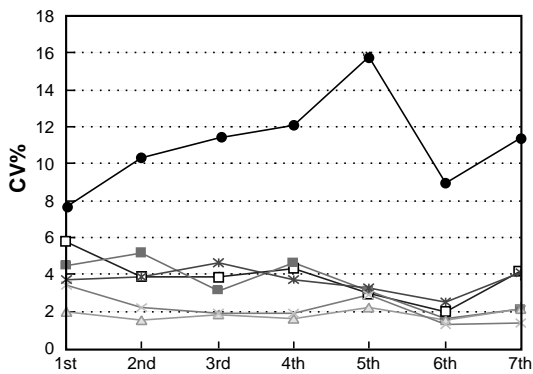


Fig. 5 Historical change of inter-laboratory CV for HGB

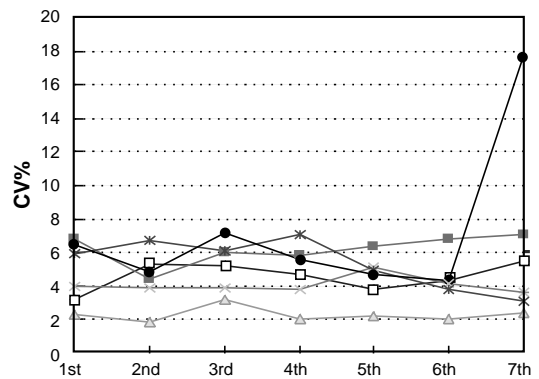


Fig. 6 Historical change of inter-laboratory CV for HCT

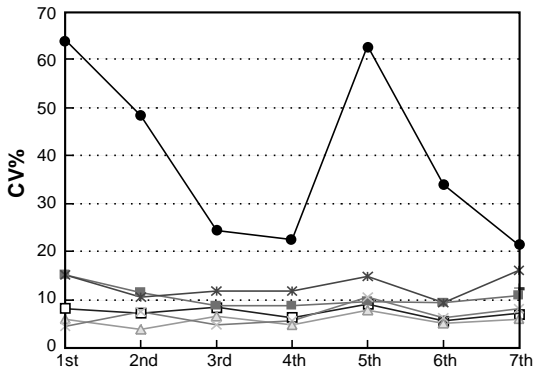
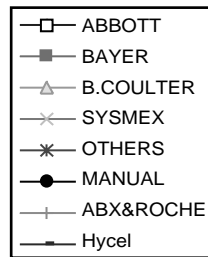


Fig. 7 Historical change of inter-laboratory CV for PLT



\*Please note that the peer group C.V. for some manufacture might be falsely elevated due to a matrix effect between the survey material and some measurement technology.

of participants. In overall tests, the performance of excellent, good, fair and poor of the university hospitals were 78, 18, 2 and 2% respectively, of the tertiary or specialized hospitals were 75, 16, 4 and 4% respectively, of the general hospitals were 73, 25, 2 and 0% respectively, of community hospitals were 70, 19, 9 and 2% respectively, of private hospitals 66, 20, 14 and 0% respectively and of military or other hospital were 64, 24, 7 & 4 respectively. The quality of hematology laboratory service in the northern region of Thailand is quite good in overall picture. However in dissected categories, there were some

hospital laboratories that need to be educated and improved their performance especially the community, private and military hospitals. Some introduced standard methods, for example platelet counting in the RBC/platelet ration method<sup>9</sup> and the ICSH recommendations for the packed cell volume<sup>7</sup>) may help us the improved results among these hospitals. Training the management of laboratory methods<sup>8</sup>) and pre- and post analytical errors<sup>9</sup>) should be included for these participating laboratory members.

*Training and education*

GSMC-EQA at Chiang Mai site had an annual meeting for our members and clinical laboratory personnel around Thailand. There were about 100 participants came to attend each meeting. Quality management concepts, laboratory accreditation followed by ISO 9002:2000, ISO/IEC 17025, ISO:DIS 15189, Thailand standard of medical technology services which was established by the Association of Medical Technologist of Thailand and the National License Committee of Medical Technologists, Hospital accreditation, cost-efficiency, cost-effectiveness and a novel concept of super quality management<sup>10</sup> were educated to our members.

*Strategies for the future*

We wish to propose the strategic activities of the EQA for the future improving the quality of the clinical laboratory to international level (Fig.8). The newsletters of the EQA and annual scientific and business meetings, workshop or training should be regularly performed. The key quality index of laboratory accreditation should be clearly established. We wish to propose the indicators for quality improvement of the clinical laboratory, i.e., percentage of pre-analytical, analytical, post-analytical errors, laboratory personnel competency of learning and growth, financial management, utilization management, risk management, customer satisfaction and results of external assessment.

**Southern region**

PSU has performed the EQA since the year 2000 at the 4<sup>th</sup> to the 7<sup>th</sup> EQA program. There are 30 laboratory participants. The percentage of responding laboratory member were varied from 75 to 93.6 %. The control of gold standard machine has been done with Mahidol University in Bangkok, Thailand and Sysmex Corporation.

**Northeastern region**

100 control samples obtained from Sysmex Corporation were sent to participants in northeastern part of Thailand

at least once a year for 3 years. The stability of control samples were monitored by gold-standard blood cell analyser (Sysmex KX 21) throughout the EQA program. The results were analyzed by Sysmex corporation and CLSC, Mahidol University for country harmonization and by the Department of Clinical Microscopy, Faculty of Associated Medical Sciences, Khon Kaen University (KKU) for regional harmonization. Examining throughout the 5<sup>th</sup> to 7<sup>th</sup> EQA program, the EQA results are at satisfactory level. Only minority of the participating members (4.76%) were out of range. These are mostly come from the district hospital.

From the results obtained, it can be seen that the results from the group with automation is well under control than the manual method as was expected<sup>2</sup>. When compared among the automated groups the results obtained using internal QC control is even better. Comparing between private and governmental hospitals, the private hospitals have better results because almost all private hospitals have automation with internal QC control.

Examining throughout the 5<sup>th</sup> to 7<sup>th</sup> EQA program, the EQA results are at satisfactory level. Only minority of the participating members (4.76%) were out of range. These are mostly come from the district hospital. Laboratory training has been suggested for this outlier group. The variations of various hematological parameters throughout the EQA program, though not much, require further investigation for the future hope of laboratory harmonization. Although the platelet counting has been better on the 7<sup>th</sup> phase EQA, the 5/76 (6.58%) were between + 2SDI and + 3 SDI, considering relatively high. Since the method of platelet count may be interfered by many factors, the platelet counting by the RBC/platelet ratio method, the ICSH reference method may be applied in future<sup>6</sup>.

**ACKNOWLEDGEMENTS**

This study has been partly supported from Mahidol University Grant. Contribution and efforts have been from many investigators from multi-centers whose name and efforts have been reported in Proceeding of the 2<sup>nd</sup>

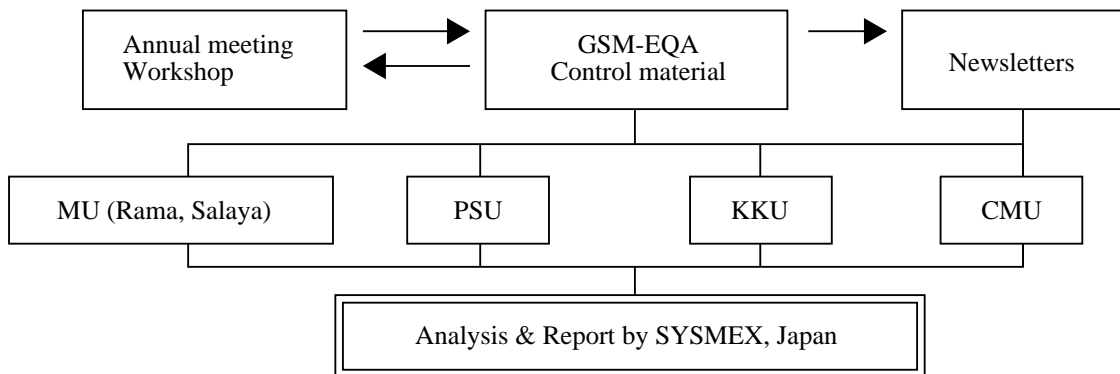


Fig. 8 Proposed activities diagram of GSM-EQA  
 (MU = Mahidol University; PSU = Prince of Songkla University;  
 KKU = Khon Kaen University, CMU = Chiang Mai University).

Annual Meeting of the GSMC-Thailand, at Chiang Mai University (CMU), Faculty of Associated Medical Sciences, October 13 –14, 2003.

**References**

- 1) Bunyaratvej A, et al.: External quality assessment of hematology laboratories in Thailand. *Sysmex J Int*, 9: 164-169, 1999.
- 2) Lewis SM: External quality assessment, In *haematology laboratory management and practice*, ed. Lewis SM, Koepke JA, Butterworth-Heinemann Ltd, Oxford, UK, 1995.
- 3) Bunyaratvej A: Laboratory accreditation in Thailand: the present status and future aspects. *Sysmex J Int*, 8: 82-85, 1998.
- 4) Bunyaratvej A: Laboratory accreditation: quality in management and analysis and the input-output control. *Southeast Asian J Trop Med Pub Health*, 30, suppl 3: 166-169, 1999.
- 5) Bunyaratvej A: Strategic plan and action plan for standardization and harmonization of hematology laboratories in Thailand. *Southeast Asian J Trop Med Public Health*, 33 Suppl 2: 83-85, 2002.
- 6) Klee G, et al.: International Council for Standardization in Haematology (ICSH) Expert Panel on Cytometry and International Society of Laboratory Hematology (ISLH) Task Force on Platelet Counting. Platelet counting by the RBC/platelet ration method: a reference method. *Am J Clin Pathol*, 115: 460-464, 2001.
- 7) Bull BS, et al.: ICSH Expert Panel on Cytometry. International Council for Standardization in Haematology (ICSH) recommendations for 'surrogate reference' method for the packed cell volume. *Lab Hematol*, 9 (1); 1-9, 2003.
- 8) Henry JB: In: *Clinical diagnosis and management by laboratory methods*, 18<sup>th</sup> ed. Philadelphia. WB Saunders, 566, 1991.
- 9) Narayanan S: Pre- and post- analytical errors. *Indian J Clin Biochem*, 11: 7-11, 1996.
- 10) Chanarat P: Productivity Improvement I: Health economic approach of super quality management as the basis for cost management. In *The Proceedings of the 9<sup>th</sup> ISQC: Global Standardization and Advanced Quality Management*, Osaka, November 3-4, 2001, p 70-72, 2001.