ORGANIZING OF NATIONAL EXTERNAL QUALITY ASSESSMENT SCHEMES IN TUMOR MARKERS (A PILOT PROJECT)

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ABSTRACT

Good external quality assessment (EQA) is necessary to the proper functioning of Thailand's tumor marker laboratories and furthermore, it is mandated by the International Standards Organization. However, international EQA schemes are not always practicable because of difficulties in transportation, communications, and financing. In fact, these schemes do not reflect the real situation of tumor marker quality in Thailand because of inappropriate performance evaluation criteria. Therefore, a pilot project EQA scheme was established by the Faculty of Medical Technology, Mahidol University.

Firstly, a number of laboratories were surveyed to establish which tumor marker tests were most commonly performed. The survey showed, in descending order, AFP, CEA, β-hCG, tPSA, CA125, CA19-9, CA15-3 and fPSA. Then the project sought to determine the quality of control materials in two forms of control materials, lyophilized and 0.2% Bronidox preserved liquid form. Both forms had two levels with different concentrations and both were kept at 4°C and at room temperature. The lyophilized serum was found to be a more appropriate sample for tumor marker detection than the liquid form.

Also, identical lyophilized sera for tumor marker testing were sent to participants six times a year and 2 specimens of 1 ml per dispatch. Participant performance evaluation was monitored by means of VIS grades A, B, C, D, F. It was found that roughly 50-60% of the participants received excellent grades for all markers. Under 10% had poor performance. The comparison revealed that the instrument provided satisfied performance for AFP is Vitros Eci, CEA and PSA for Beckman Access, CA125, CA15-3, CA19-9 and β-hCG for BM Elecsys. However, unsatisfactory performance was observed for AFP, CEA and β-hCG by Cobas core, PSA, CA125, CA15-3 and CA19-9 for Abbott AxSYM.

In conclusion, the pilot project was an initial attempt to establish an EQA scheme for tumor markers in Thailand. It has discovered some possible problems in instrument performance which it would be worthwhile to investigate further.

KEY WORDS: / EXTERNAL QUALITY ASSESSMENT / TUMOR MARKERS / CONTROL MATERIAL

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โครงการจัดตั้งองค์กรประเมินคุณภาพการตรวจสารบ่งชี้มะเร็ง (ORGANIZING OF NATIONAL EXTERNAL QUALITY ASSESSMENT SCHEMES IN TUMOR MARKERS (A PILOT PROJECT)

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บทคัดย่อ

การเข้าร่วมโครงการ EQA เป็นหนึ่งในมาตรฐานคุณภาพตามข้อกำหนดของ ISO แม้ว่าปัจจุบันมีหน่วยงานในระดับนานาชาติที่ให้บริการประเมินคุณภาพห้องปฏิบัติการอยู่เป็นจำนวนมาก เช่น UK NEQAS, RIQAS, RCPA ฯลฯ แต่ก็มีจุดด้อยในการเข้าร่วมโครงการกับองค์กรต่างประเทศคือ ความไม่สะดวกในการติดต่อสื่อสาร, การขนส่งตัวอย่างกินเวลานานจึงเสี่ยงต่อการเสื่อมสภาพและสูญหาย, มีค่าใช้จ่ายสูงทำให้ต้องเสียเงินตราต่างประเทศเป็นจำนวนมาก ยิ่งกว่านั้นเกณฑ์การประเมินของโครงการในระดับนานาชาติยังไม่เหมาะสมกับสถานการณ์ในประเทศไทย ดังนั้นองค์กรประเมินคุณภาพการตรวจสารบ่งชี้มะเร็ง โครงการนำร่องของคณะเทคนิคการแพทย์ มหาวิทยาลัยมหิดล จึงจัดตั้งขึ้นเพื่อเป็นอีกทางเลือกหนึ่งของห้องปฏิบัติการที่สามารถเข้าร่วมเป็นสมาชิกโครงการประเมินคุณภาพ

การศึกษาโครงการนำร่องนี้แบ่งออกเป็น 2 ส่วน คือ การออกแบบสอบถามเพื่อศึกษาสภาพการการตรวจสารบ่งชี้มะเร็งและความเป็นไปได้ในการจัดตั้งองค์กรฯ การศึกษาเสถียรภาพและเลือกตัวอย่างตรวจที่เหมาะสมสำหรับโครงการ ต่อจากนั้นจึงดำเนินโครงการประเมินคุณภาพการตรวจสารบ่งชี้มะเร็งโดยองค์กรภายนอก (โครงการนำร่อง)

ผลการสำรวจจากห้องปฏิบัติการ 70 รายพบว่าการทดสอบที่เปิดให้บริการส่วนมากคือ AFP (65 แล็บ, ร้อยละ 92.9), CEA (62 แล็บ, ร้อยละ 88.6), β-hCG (46 แล็บ, ร้อยละ 65.7), tPSA (45 แล็บ, ร้อยละ 64.3), CA125 (20 แล็บ, ร้อยละ 28.6), CA19-9 (17 แล็บ, ร้อยละ 24.3), CA15-3 (15 แล็บ, ร้อยละ 21.4), fPSA (5 แล็บ, ร้อยละ 7.1) ในจำนวนนี้พบว่ามีเพียง 7 แล็บที่เป็นสมาชิกในองค์กรระดับนานาชาติและมีถึง 54 แล็บต้องการเข้าร่วมโครงการของเรา

การศึกษาเสถียรภาพของตัวอย่างตรวจ 2 ชนิดคือตัวอย่างในรูปแห้งและในรูปน้ำที่มี Bronidox อยู่ร้อยละ 0.2 เป็นสารรักษาสภาพ พบว่าตัวอย่างตรวจในรูปซีรั่มแห้งมีความเหมาะสมที่เตรียมเป็นตัวอย่างตรวจสารชี้บ่งมะเร็งซึ่งมีเสถียรภาพได้นาน 60 วัน ณ อุณหภูมิ (34 - 42° C)

การดำเนินโครงการประเมินคุณภาพการตรวจสารบ่งชี้มะเร็ง (โครงการนำร่อง) มีสมาชิกเข้าร่วมโครงการ 72 ราย โครงการจัดส่งซีรั่มแห้งปริมาตร 1 ml ให้สมาชิก 6 ครั้ง /ปี โดยแต่ละครั้งส่งตัวอย่างจำนวน 2 ขวดรวมทั้งสิ้น 12 ตัวอย่าง / ปี หลังจากสิ้นสุดโครงการ ระบบคะแนน VIS ถูกนำมาใช้ประเมินประสิทธิภาพในการตรวจสารบ่งชี้มะเร็งโดยแบ่งออกเป็น 5 ระดับคือ A, B, C, D, F พบว่ามีห้องปฏิบัติการที่มีประสิทธิภาพโดยรวมในระดับดีมากอยู่ร้อยละ 50.7 ในการตรวจ AFP, ร้อยละ 61.9 สำหรับ CEA, ร้อยละ 52.9 สำหรับ PSA, ร้อยละ 62.9 สำหรับ CA125, ร้อยละ 65.2 ใน CA15-3, ร้อยละ 58.7 ใน CA19-9 และร้อยละ 61.2 ในการตรวจ β-hCG ระดับค่าเฉลี่ย MVIS ของการตรวจ AFP, CA19-9, β-hCG ตั้งแต่เริ่มจนสิ้นสุดโครงการมีแนวโน้มคงเดิมจึงต้องการเวลาในสังเกตเพิ่มขึ้น ส่วน CEA มีแนวโน้มเพิ่มขึ้นแสดงถึงประสิทธิภาพการตรวจ CEA มีแนวโน้มเลวลง แตกต่างกับ PSA, CA125, CA15-3 มีแนวโน้มลดลงแสดงถึงประสิทธิภาพการตรวจดีขึ้น ในการประเมินประสิทธิภาพเครื่องมือวิเคราะห์พบว่าเครื่องที่มีประสิทธิภาพดีในการตรวจ AFP, CEA, PSA คือเครื่องที่อาศัยหลักการ ICMA (% CV ร้อยละ 5.7, 6.7, 5.9) และเครื่องที่มีประสิทธิภาพดีในการตรวจ CA125, CA15-3, CA19-9, β-hCG ได้แก่เครื่องที่อาศัยหลักการ ECLIA (%CV ร้อยละ 4.3, 6.7, 5.5, 4.8) ซึ่งเครื่องดังกล่าวมีความแปรปรวนต่ำกว่าความแปรปรวนที่ยอมรับได้ซึ่งคิดจากค่าเฉลี่ยความแปรปรวนในระหว่างการดำเนินโครงการในระยะเวลา 1 ปี CA125, CA 15-3 and β-hCG (CV ร้อยละ 7.6), CEA (CV ร้อยละ 8.0), CA19-9 (CV ร้อยละ 8.3), PSA (CV ร้อยละ 9.2), AFP (CV ร้อยละ 9.5)

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LIST OF ABBREVIATIONS

Abbreviation of symbol

ACD	Enriched acid citrate dextrose
AFP	Alpha-fetoprotein
ALT	Alanine aminotransferase
ALTM	All lab trimmed mean
Anti HBC	Anti Hepatitis C virus antigen
Anti HBs	Anti Hepatitis B virus surface antigen
Anti HIV	Anti Human immunodeficiency virus
ANOVA	Analysis of variance
AON	Average of normals
AST	Aspartate aminotrasferase
AxSYM/IMX	It is an autoanalyzer trademark of Abbott Co.,Ltd.
β	Beta
Beckman Access	It is an autoanalyzer trademark of Beckman Coulter, Inc.
BIS	Bias index score
BIAS	Cumulative bias
CA125	Cancer antigen 125
CA15-3	Cancer antigen 15-3
CA19-9	Cancer antigen 19-9
CCV	Chosen coefficient of variation
CDC	Center for disease control
CEA	Carcinoembryonic antigen
CLIA	Clinical laboratory improvement Act
Cobas core	It is an autoanalyzer trademark of Roche Co.,Ltd.
CPD	Citrate phosphate dextrose
CV	Coefficient of variation
DPC immulite	It is an autoanalyzer trademark of DPC Co.,Ltd.
DV	Designated value

LIST OF ABBREVIATIONS (Cont.)

Abbreviation of symbol

ECLIA	Electrochemiluminescence
EDTA	Ethylenediaminetetraacetic acid
ELFA	Enzyme linked fluorescent immunoassay
Elecsys	It is an autoanalyzer trademark of Roche Co.,Ltd.
EQA	External quality assessment scheme
EQAT	External quality assessment scheme in tumor marker
HAMA	Human anti-mouse monoclonal antibody
Hb	Hemoglobin
HBsAg	Hepatitis B virus surface antigen
hCG	Human chorionic gonadotropin
ICMA	Immunochemiluminometric assay
IQC	Internal quality control
ISE	Ion selective electrode
IU	International unit
IUPAC	International Union for Pure and Applied Chemistry
kDa	Kilodalton
KU	Kilounit
L	Liter
mAb	monoclonal antibody
MEIA	Microparticle enzyme immunoassay
min	Minutes
MIS	Misclassification index score
ml	Milliliter
NCEP	National cholesterol education programme
NEQAS	National external quality assessment scheme
ng	Nanogram
PCV	Packed cell volume
POCT	Point-of-care-testing
PSA	Prostate-specific antigen

LIST OF ABBREVIATIONS (Cont.)

Abbreviation of symbol	
RBC	Red blood cell
RCPA	Royal college of pathologists of Australasia
RCV	Reference change value
RIQAS	Randox international external quality assessment scheme
SEKK	Czech Republic external quality assessment system
SD	Standard deviation
SDI	Standard deviation index
UK	United Kingdom
UK NEQAS	United Kingdom national external quality assessment scheme
μg	Microgram
US	United state of America
Vidas/minividas	It is autoanalyzer trademark of Biomerieux Co.,Ltd.
VIS	Variance index score
Vitros Eci	It is autoanalyzer trademark of Johnson & Johnson Co.,Ltd
WBC	White blood cell count
WEQAS	Wales external quality assessment scheme
WHO	World health organization
° C	Degree celcius
%	Percentage

CHAPTER 1
INTRODUCTION

Cancer is a growing problem throughout the world and is ranked secondly behind heart disease as a cause of death (1). The estimate number of new cases each year is expected to rise from 10 millions in the year 2000 to 15 millions by 2020 (2). In Thailand, with the high incidence of liver cancer (37.4/100 000) in male and cervical cancer (23.4/100 000) in female, several attempts to deal with cancer have been developed those are; 1) preventing exposure to the cause of cancer, 2) early disease detection, and 3) development of more effective therapeutic modalities. The first approach seems to be the best way (3,4). Unfortunately, it is unrealistic and difficult to avoid exposure to all environmental and biologic cancer associated risk factor. Therefore, early detection is the most promising approach. Many tumor markers are assayed to detect cancer in medical laboratory for cancer diagnosis, staging, monitoring, evaluation of response to therapy, detection of recurrent disease. Since cancer is the disease that effect not only the patient' s health but also the patients psychology, so reliable result is very important. In tumor marker assay, there are many factors influencing to the test results; three main groups of unavoidable variations namely pre-analytical, analytical, and post-analytical variation affects the quality of results (5). Apart from pre and post-analytical variation, tumor markers testing always suffers from high dose hook effect, specimen carry over, interference from heterophilic or human anti-mouse antibodies (HAMA) in analytical process (6). In addition, with an increasing number of inventing of many methods/kits to the market recently, which is a cause of differing antibody specificities, assay robustness, variation in reference range among methods/kits. All of them leads to give discrepancies in results obtained from different manufacturers or different laboratories, so these results can not be used interchangeably. Fraser CG has established the desirable quality specification (CV_A) for CEA, PSA, CA125, CA15-3, CA19-9. Its %CV is 4.7 for CEA, 7.0 for PSA, 6.8 for CA125, 2.9 for CA15-3, and 12.3% for CA19-9 (7). As a resulted of surveyed in many countries, no one can meet this criteria.

The CV_A of AFP is 16.2% in Australia, CEA is 35% in Italy, PSA is 37.7% in German, CA125 is 15.8, CA15-3 is 14.7, CA19-9 is 27.2 in France (8,9,10,11). This large inter-laboratory variation affect laboratory precision and eventually accuracy of report results caused physician misdiagnosis of disease, so laboratory extremely need to improve their performance to provide reliable result. One type of quality system namely external quality assessment (EQA) was used as a tool to accomplish this aim. An example of advantage of implementing of EQA scheme in Italy, Zucchelli CG et al reported that there is a significant reduction of the CV_A of the CEA assay from 35% in 1985 to 20-25% in 1991 (12). In United Kingdom (UK), there is an improvement of %CV of AFP from 16% in 1977 to 10% in 1980 after implementing an EQA scheme (13).

Nowadays, there are many international tumor marker EQA schemes enable oversea countries to participate; however, participation in oversea scheme have two major drawbacks; in social reason and analytical reason. In social reason, it is expensive, time consuming, risk of material denature under improper temperature, take a troublesome and lead to lost of oversea currency to participate in oversea scheme, and international schemes emphasized primarily on participant in their own country. In analytical reason, each of country has different situation. Developed countries have highly efficient automated workplace, and advance system of quality control, so an error can be easily maintained as small as possible. In contrast, in developing country where work with manual techniques, it is difficult to decrease such error, so the level of quality specification of different type of country must be difference (14). It is difficult for developing countries to keep quality as the same as in developed countries. The developed countries must have stringent CV_A more than those of developing countries. Moreover, the need of criteria for acceptable laboratory performance is different, so state-of-the-art in their own country should be established by their own EQA (15). As the medical laboratory play a major role in cancer disease. Therefore, tumor marker EQA scheme should extremely be introduced for improving a laboratory performance, reducing inter-laboratory variations and established state of the art in tumor maker assay in our country.

CHAPTER 2
OBJECTIVE

To set up a pilot for an external quality assessment of tumor markers (EQAT) and monitor participant laboratories performance

CHAPTER 3
LITERATURE REVIEW

1. Quality system definition

Nowadays, Health care providers face ever increasing pressure from both politicians and consumers to provide high quality health care that why the quality system must be established (16,17). Simply speaking, the term “Quality” is a conformance to requirement (18). Strictly speaking according to International Standardization Organization (ISO) definition, the term “Quality is a totality of feature and characteristics of a product or service that bear on its ability to satify stated or implied needs”. The quality system made up of the following components : 1) Good laboratory practice (GLP) concerned with the organizational process and the conditions under which laboratory studies are planned, performed, monitored, recorded, and reported". GLP prescribes a laboratory to work according to a system of procedures and protocols. 2) Quality management is the assembly and management of all activities aimed at the production of quality by organizations of various kinds. It can be considered as a modern version and meaning wider than that of GLP (19). 3) Quality assurance (QA) is the essential organizational infrastructure that underlies all reliable analytical measurements. It is concerned with achieving appropriate levels in matters such as staff training and management, adequacy of the laboratory environment, safety, the storage, integrity and identity of samples, record keeping, the maintenance and calibration of instruments, and the use of technically validated and properly documented methods (20). 4) Quality planning (QP) is the system focus on customers, emphasizes, the importance of understanding their needs and expectations and leads to the definition of quality goals which guide the planning of new processes when failure in quality goals. 5) Quality improvement (QI) is the system providing the structural mechanisms necessary to solve problems that extend across laboratory sections or extend to related health care practitioner (21). 6) Quality control (QC) is the operational techniques and activities that are used to satify quality requirements. Two more term conducts in analytical phase of quality control are

internal quality control (IQC) and external quality assessment (EQA). IQC are set of procedure undertaken by laboratory staff for the continuous monitoring of operation day by day checking of the produced data to decide whether results are reliable enough to be released. It can reject errors at the first step which may lead to correction of the error; and thereby, to improvement of analytical quality. EQA is the retrospective system of objectively accessing and evaluating the laboratory performance by an outside agency, including comparison of a laboratory's result at intervals with those of other laboratories (22). EQA is a complementary tool with IQC to monitor laboratory performance, not to replace it. Total quality management (TQM) and continuous quality improvement (CQI) quickly replaced the QA modal because of its expanded emphasis on satisfying the needs of customer, each unit within the organization had to successfully perform, and meet the obligation of customer, producer and supplier. This process helps to correct a major deficiency of QC and QA by providing tools with which to identify and troubleshoot problems that might occur at each stage of production (23).

2. Internal quality control

There are many IQC techniques varied from advance to traditional IQC techniques. An example of advance one is the use of Six Sigma which has been in use since the 1980s. The philosophy behind Six Sigma is that there is a direct correlation between the number of product defects, waste operating costs, and the level of consumer satifaction. It mean that once a Sigma increase, the reliability of process improves, operating cost go down, and the consumer satifaction increase. Another one is the traditional one; that is the use of correlation of laboratory test results, delta checks, Bull's algorithm, average of normals (AON) and QC chart. Comparing the relationship between laboratory test results is considered as one type of IQC in common sense. Common examples are the use of anion gap, scenarios of direct bilirubin greater than total bilirubin, serum albumin greater than total protein, grossly abnormal ALT with normal AST, significantly increased creatinine with normal urea nitrogen. That remaining one are statistical base-IQC, The delta checks, it emphasizes on the detection of laboratory errors, particularly those due to specimen mix-up or specimen alteration due to dilution by intravenous fluid. This technique detected error

by comparing the current laboratory test results with values obtained on previous specimens obtained from the same patient (24). Another one, Bull's algorithm was established in 1974 by Bull et al (25). This technique designed to assess quality control of erythrocyte indices, and was widely incorporated into commercial hematology analyzers. Bull's algorithm is based on the recalculation of a new patient mean from a preexisting mean following the analysis of usually 20 samples. A calculated function ,d, is added to the old mean to calculate the new mean. An average not within its 3% limits, or 0.97 to 1.03 times the accepted stable patient mean, would require appropriate correction action. For AON, it was first introduced in 1965 by Hoffman and waid. The assumption underlying the average of normals is that the patient population is stable. The AON use tracking patient medians and the 25th and 75th percentiles as a truncation limits to set up control limit. In a day, the patient result falling within the control limits are averaged and compared with the control limits previously established. If the average falls outside the control limits, the process is considered to be out of control. Even it is not out of control, Any shift would thus be secondary to a systematic analytical error. The power function to error detection of AON depended on the number of patient results averaged and the ratio of standard deviation of the patient population to the standard deviation of the analytical method, control limits, truncation limits, and the magnitude of the population lying outside the truncation limits. The last one is IQC chart, It can be divided into 2 major technique; Cusum (cumulative summation) techniques and Shewhart chart technique (26). Because it is easy to manual calculate and available in automate system, it is a popular one now in use. This technique has been adopt for many years; in 1950 Levey and Jennings introduced into the clinical laboratory; in the early 1980s Westgard established the QC rule by using computer simulation model. The philosophy of Westgard QC rule is the rule must have high probability of error detection and low probability of false rejection. Now, the most frequently used Westgard rules and the nomenclature used to identify the particular rule are as follows: 1:2s; it means one control value exceeds the mean by ±2SD, 1:3s; it means one value exceeds the mean by ±3SD, 2:2s;it means two consecutive control values exceed the same mean by ± 2SD, R:4s, it means one control value exceeds the mean by +2SD and the other control value is less than –2SD from the mean, 4:1s; it means four consecutive values

for the same level of quality control material exceed the mean by +1SD or by –1SD, 10:x; it means ten consecutive control value for the same level of quality control material occur on the same size of the mean and 7:T; it means seven consecutive control values showed increasing or decreasing trend in subsequent values. It can be summarized using 1:3s and R:4s rule are suitable for detect random error, in contrast, 2:2s, 4:1s,10:x and 7:T rule are suitable for detect systemic error. Even though laboratories are fully computerized and quite capable of implementing all Westgard rules, most US laboratories use only 1:2s, 1:3s and R:4s (27,28).

3. External Quality Assessment

The birth of EQA scheme was first noted since Belk and Sunderman created EQA scheme in US in 1946, After that time, many EQA schemes have rises up over time together with the arise of many synonyms of EQA such as interlaboratory QC, external surveillance, surveys, proficiency testing (PT) and external quality assessment (EQA) (29). Among these terms, the first three terms is general word. The term “round robins” use by Gunter EW et al (1996) for serum and whole-blood folate external proficiency testing survey (30). The term “EQA” is used in Europe and Asia. The term “PT” is used in America. Even though its name is difference, they shares common components those are 1) selection of control material, 2) distribution of material to participating laboratory, 3) analyzing of the material, 4) data evaluation, 5) report result to participant. To set up EQA scheme, it should be started from the situation analysis of laboratory service to gather necessary information such as the number of laboratories, type, principle of measurement in order to define the possibility to set up EQA scheme. If there is a possibility to set up an EQA scheme. Next step, the organizer invited laboratories who need to participate enrolled in EQA scheme. Participating laboratories are identified by a code known only the organizer. Then, control materials are distributed on a regular schedule. After that, participants analyze and report result to organizer. Then, results are subjected to statistical analysis, and the performance of individual laboratory is assessed. Laboratories who are poor performance were advice by program committee to improve their performance (31).

In the past, the goal of EQA is limit only inter-laboratory comparison. Nowadays, with an evolving to a broad scope of activity, Thomas A (2004) stated that the goals of

modern EQA scheme are also expanded those are; 1) participant performance evaluation, 2) method performance evaluation, 3) post-market vigilance, 4) training and help. In the participant performance evaluation, it can be divided into 10 sub-elements following as : 1) quality of analytical performance of the participant's laboratory, 2) the state-of-the-art of participating laboratory, 3) Intra-laboratory variation, 4) Inter-laboratory variation, 5) relationship between calibration procedures and analytical results, 6) relationship between analytical procedures and results, 7) relationship between commercial reagents and results, 8) relationship between analytical instruments and results, 9) state-of-the-art values for concentration of the analytes, 10) systematic deviations for the individual laboratory from state-of-the-art values or reference target values. Among these, some of these points are overlap. A well-designed EQA scheme should provide information on all points. A passage of step to completed the goal was that in while the manufacturers invented their technologies into market, the manufacturer's established performance claims in the area such as precision, accuracy, linearity. EQA organizer not only laboratory performance were evaluated by compared with other laboratories, but also method performances were evaluated. An example were found in UK NEQAS Steroid hormone, WEQAS Mainline chemistry, and WEQAS lipid scheme to investigate the effect of a turbid sample on performance of lipid analysis by using grossly lipemic non-filtrated pool sera. If the method suffer from lipemic sera effect, it is a manufacturer responsibility to improve their technologies in post-market vigilance such as non-appropriate cut-off values and reference range in package insert, non-specific reactions in a particular batch of reagent and calibration error. Finally, all knowledge obtained from participant in EQA scheme can be used for continuous education, training and help. An example of this is in sodium assay by all ISE method using the same reference range. A knowledge from EQA reveal that the direct and indirect ISE give different results (32). Ultimately, effort has been made by manufacturer to solve this problem. As a knowledge from EQA, now, in sodium assay, direct and indirect ISE were manipulated to use the same reference range. In third world countries; however, the progress of quality assurance activity is quite slow when compare with developed countries, so EQA scheme in Asia are not provide completed those points (33).

3.1 Selection of control material

In order to draw right conclusion from EQA results, quality of EQA sample is essential. Organizer must provide appropriate control material. When considering control material, two term always consider those are “analyte” and “matrix”. The analyte is defined as a substance or property to be measure. The matrix is defined as an analytical bias due to the matrix of the processed specimen being measured (34). The matrix of control material must have behavior as closely mimic patient material. There are three types of matrix; human-based, animal-based and artificial-based matrix. Each of them has different advantage and disadvantage. The human-based matrix has behavior similar to patient material but there is a risk of infection, and sometimes difficult to obtain sufficient volume. All modern EQA schemes prefers to use this type of control material. The animal-based matrix also risk to disease transferable to man but in limit (35). It is generally use in tradition EQA scheme i.e. Wiener K (1980) use this type of control material in regional quality control program for salicylate and paracetamol (36). The artificial-based matrix is easy to prepare and no known risk of infection. It is usually used a control in POCT devices. The disadvantage of the use of animal and artificial-based matrix are the non-commutability; so it losses in the ability to show inter-assay properties comparable to those of patient material and traceable link between patient sample results and standards (37). Francini C et al (1993) derived the protocol for assessing the commutability of EQA serum (38). The processing steps in the preparation of control material are following as 1) collecting materials, 2) filtration, 3) spiking, 4) filling. In collecting material process, sometimes the additives were added in special purpose i.e for sterile preservation, Seth J et al (1988) use 0.1% sodium azide in growth hormone EQA scheme in UK (39). Gunter EW et al (1996) add L-ascorbic acid to stabilized folic acid in serum during storage (30). There are some specially collected samples in some EQA schemes i.e. New York state PT program use human female serum for PSA testing. The raw material may be obtained from single donations or the discarded patient sample, the advantage of discard material is that it is not concerned with consent from donation but there is disadvantage to take a long time to collection resulted in more hemolysis or turbidity from deterioration of material. In single donation material, Stock et al (2003) recommend that single-donation serum could be

used in EQA sample (40). The advantage of this is to reduce the effect of non-commutability or unpredicted interference. However, the limitations due to specimen volume which may restrict the statistical sample of particular method, the cost of materials and the difficulty of single-donor specimens to monitor a large number of measurands are concerned. In biochemical and serological test, the sera or converted plasma can be used. If sample collects from blood donation, blood elements are removed by centrifugation at 2500xg for 20 minute. Calcium chloride or thrombin is added and let to coagulate by incubating at 37° C for 90 minute or until complete clot is achieved and the clot is removed by centrifugation at 13000xg for 20 minute (41). However, the speed and time to centrifuge are varies. Baadenhuijsen H et al (1995) centrifuge at 3000xg for 30 minute to remove chylomicron. WHO's regional office for South East Asia offer 3500xg for 10 minute (42,43). To prepare control material in hematology purpose, the use of EDTA-anticoagulant human blood is stable for only 24 hours for RBC, PCV, so it can be used in a scheme that no great number of participant. The whole blood preserved with ACD or CPD can be used for RBC, PCV, Hb, WBC. In blood coagulation, heparinized plasma was used (44). After the amount of raw material is enough, samples must be tested to exclude risks of infections for hepatitis and HIV. A typical panel, used for testing commercial control serum is: anti-HAV, anti-HBc, HbsAg, anti-HCV, anti-HIV I/II . The pools are sometimes heated at 56° C for inactivation of HIV antigens or using 1% w/w tri(n-butyl)phosphate (TNBP) and Triton X-100 and incubate the pool at 30° C for 4 hours to inactivate viruses in pools. The screening negative control material must then be filtrate to reduce lipoprotein concentration and remove contaminating bacteria formed during storage, using Millipore filters, with sequential passage through a 5.0 μm and finally a 0.22 μm (21). However, control material for blood count parameter use only 40 μm filter. In contrast with urine pool, it is not need to be filtrated. The next step of preparation control material is a spiking procedure. It is commonly use in biochemical test to modified the concentration of analyte in control material. The spiking substance may be endogenous or exogenous substance. An example to use exogenous substance is in drug monitoring scheme in UK; however, these samples give only simplistic mimetic real human patient's samples. They do not allow an evaluation of cross –reactivity with metabolites, and it may be difficult to mix the quantity homogeneously into the

basic material, the specifications of the quantity added may not represent that found in patient's material. For the addition of endogenous substance i.e. Middle JG (1990) in EQA for cortisol, progesterone, estradiol, testosterone and 17-hydroxyprogesterone in UK, This type of additive is often used in substance which is expensive to purchase standard; however, it is risk to the no guarantee that the material is effectively free from interference and undesirable effect (45). In case of blood count control material, the spiking is not necessary. Only the fixative agent to stabilized whole blood was added. Srisarin A et al (1999) added 1 part of fixative containing formaldehyde, glutaraldehyde, trisodium citrate, to 50 parts of blood (46). When getting desirable concentration of control material, filling control material into vial must be controlled for reproducibility in dispensing material into vials. The reproducibility should have a CV of 0.5% to 1%. It is depend on the volume of control material that allow for uncertainty of pipetting. After finished filling process, in case of biochemical test, the control material will be frozen to prepare a frozen form, or fresh to prepare a liquid form, or freeze-drying to prepare lyophilized form. Each EQA scheme choose different form. Frozen pooled serum can be prepared by it own laboratory. It is the cheapest one, the viscosity and turbidity are not change from original serum. However, the Frozen pooled serum seems to be non popular type of control serum in EQA because of there are many limitation i.e. difficulty for dispatched to participant, danger of contamination. It is limit only using for IQC propose. However, Penno G et al (1990) report the used of frozen urine as a control material in EQA for urinary albumin radioimmunoassay (47). The liquid control material seem to be the most suitable control material. Sturgeon CM et al (1990) used the liquid human sera as a control material in EQA scheme for CEA and hCG (48). However, there is a stability limitation. To solve that scheme, control material should be added with preservation to extend the stability i.e. Ethanediol, Ethylene glycol. However, the stabilizer may be interference in assay itself. Devleeschouwer N et al (1994) reported the positive interference of metrthiolate in the TDx digoxin assay in control samples used in Belgian EQA scheme (49). The other choices is to use lyophilized control material. It is stable up to 2 years when dry. Guder WG et al (2000) report the use of lyophilized urine as a control material of urine analysis in Spain and Italy (50). However,

lyophilization can cause changes in physico-chemical properties of proteins which can affect their chemical reactivity in an analytical method.

3.2 Freeze-Drying technique

The terms freeze-drying and lyophilization can be used interchangable. Freeze-drying was first carried out by Altmann, who freeze-dried organ pieces in 1890. The freeze-drying or lyophilization is a drying process, in which the solvent and/or the medium of suspension is crystallized at low temperatures and thereafter sublimated from the solid state directly into vapor phase. The most important goal of freeze-drying is to produce a substance with good shelf stability. The freeze-drying process consists of two major steps: freezing of solution, and drying of the frozen solid under vacuum. The drying step is further divided into two phases: primary and secondary drying. The primary drying removes the frozen water and the secondary drying removes the frozen bound water. In freeze-drying process, freezing step is the first step, it can be conducted in the freeze-dry apparatus or in a separate apparatus. The product must be cooled to such a temperature at which the water and the solids are fully crystallized, or at which areas of crystallized ice and solid are enclosed in zone in which amorphous concentrated solids and water remain in mechanically solid state. The sample morphology; the size, location and orientation of the ice crystals formed by the freezing process, depend on several factors i.e. cooling velocity, initial concentration, end temperature of cooling, and the time at this temperature. In case of slower freezing rate, it gives a small number of large ice crystal which tend to be more oriented in one direct. In contrast, rapid freezing give large numbers of small ice crystals which are not oriented in one direction. The samples with smaller crystals and disoriented crystals will tend to have a higher resistance to mass transport in the sample during drying process. The product become low quality. After freezing process completed , the drying process continue. This process are governed by two transport mechanism; mass transport and heat transport. In mass transport, it is the movement of water. the heat energy, transmitted from heater to sample chamber, is required to transform the ice into water vapor; it is a process of heat transport. During the water vapor occurred, there exits a pressure difference between sample holder and condenser leading the water vapor transported into the drying chamber to become condensation

due to the effect of mass transport. The good freeze-dry instrument must have large difference in temperature and pressure between condenser and sample holder. However, there are limits to the temperature and pressure differences that can achieve because, in practice, is limited by the material's melting properties and, in theory, there are no perfect pump so the condenser cannot have a lower pressure than absolute zero. There are many factor involve in quality of product in freeze-drying process. For example, During the freezing process, it generates low temperature stress. An example of low temperature stress of incubation under -40° C of frozen ovalbumin solution caused structural change. Moreover, low temperature stress can generate an indirect effect to sample; i.e. concentration effect, pH changes during freezing. To protect protein from freezing, a protein stabilizer may be used i.e. sugar/polyols, polymers, protein itself, Non-aqueous solvents, surfactants, amino acids. The mechanism of cryoprotection is preferential interaction. The stabilizer prefers to interact with water(preferential hydration) to excluded protein from the surface of solution. In drying process, because there are no hydration shell of proteins so the preferential interaction mechanism is no longer work. The mechanisms of lyoprotection is the formation of an amorphous glass during drying. Formation of amorphous glass increase protein stability by slowing down interconversion of conformational substrates and conformational relaxation of a protein. Because the viscosity of amorphous more than crystal form, drying sample in amorphous form protect protein in drying step. The another mechanism involve with stabilizer forming hydrogen bonds between a protein and stabilizer at the end of the drying process that is a preference requirement of polar groups on the protein surface. Nowadays, the infrared spectroscopy is the most common method for monitoring protein denaturation upon lyophilization(51,52,53,54).

3.3 EQA runs

The frequency of EQA runs and the number of sample each run varies between EQA schemes, It is depends on the difficulty in executing effective analytical QC, laboratory throughput of analyzes, consistency of results from previous rounds, cost benefit of the scheme, and availability of suitable materials for test scheme and reflected the needs of the scheme. The test having a high throughput of patient's

sample should be run EQA scheme more frequency than the others; however, the number of sample can be adjusted with reflected the frequency of EQA run (31). In general, the number of EQA cycle could be found on 2, 3, 4, 6, 8, 10, 11, 12, 24 distribution per year. Independently, the number of sample could be found 1, 2, 3, 4, 5, 12 per time. Its difference due to the strategies of each scheme. For example, with the number of 24 samples equally, RIQAS immunology scheme dispatch 2 time per year but the number of sample each dispatch is 12 (55). They request their participants analyse in turn every fortnight. However, cardiac marker WEQAS scheme dispatch 12 times per year, and the number of sample are 2 per dispatch (56). Observably, the number of sample reflect the data evaluation. In the view of IUPAC, ISO and AOAC, the optimal frequency is probably between once in 2 weeks and once in 4 months. A frequency greater than once in 2 weeks would for most biomarker analyser seem not to be cost effective; it would also encourage replacement of IQC by EQA (31). In addition, there are two interesting strategies are to use the two samples, evaluate test result by adapted multirule system to SDI, and the use graphical Youden plot of pair samples. The adapted multirule system can be seen in PT result evaluation. An example of the use of Youden plot can be seen in RCPA by plot of the low concentration specimen against the high concentration specimen. If the laboratory pair of results are in acceptable, the point will be in the central square (57).

3.4 Evaluation of results

Performance evaluation criteria of participating EQA scheme are based on biological variation, opinions of experts, state-of-the-art, or statistical limit. Each country used different criteria and sometimes also varies in great extent detail. The acceptability limit of biological variation based on clinical use of laboratory data. Fraser GC et al elucidate the desirable standards for analytical performance in view of biological variation. The laboratory' s CV_A and deviate value from true value must be less than that criteria. The opinions of experts criteria is usually used in those of microbiology, blood banking, and microscopy as a referee. It is always introduced couple together with the consensus of participant. The state-of-the-art survey usually come from the acceptability limit that 20% of laboratories will meet them i.e. for cholesterol, NCEP guideline that the acceptability bias is $< \pm 3\%$ and CV $\leq 3\%$. In

fixed limited, it is usually use as a criteria of CLIA'88 in PT in US (58). Some schemes, The rarely seen approach to assess the participants performance are used; i.e the calculation of the performance rating described by Reed SE et al (1985).This rating is the number of standard errors that differ from the mean the performance index (PI) described by Naka H (1995). Another one is the scoring point for laboratory performance obtained by expressing the difference between the result obtained and the designated value in terms of the standard deviation, squaring this number and subtracting it from 10 described by Tan IK et al (1984) (33,59,60). In general, there are three types of data can be seen in EQA scheme; nominal scale in qualitative tests, rough estimates on an ordinal scale in semi-quantitative tests, ratio or interval scale in quantitative test. Each type of data have different strategies to evaluation. For Quantitative tests, the ordinary parametric test provide the estimation of central location and spread of result. If the data are normal distribution, Mean, SD, %CV were calculated (outlier exclusion), unless, the median, interquartile range, %CV were used instead (35). This type of statistical evaluation always use in every quantitative schemes to access the group performance. To evaluated individual laboratory performance, the special scoring system must be introduce and this is different in each scheme. Firstly, the target value and limit of acceptability of results must be established. There are many ways to establish target value: (1) target value obtained with a reference method, (2) method dependence target value, (3) method independence target value. It is all accept that the target value obtained from reference method is a most confidential target value because it provide accuracy assessment (58). This type of target value usually provide by international scheme such as UK NEQAS, RIQAS, RCPA, SEKK if reference method is available. With the limitation of reference method, the consensus value was used instead. The consensus value can be divide in to two types; method dependence and method independence consensus value. The use of method dependence have an advantage to make a big group for reliable results and it can be assess the method bias if there is a huge deviated from that consensus of individual. The advantage of the use method independence consensus value is to provide laboratory performance picture related to instrument/reagent/calibrator/control used. Nowadays there are 4 widely use scoring

systems in quantitative report; 1) VI scoring system , 2) SDI scoring system , 3) ABC scoring system , 4) MIS scoring system

3.4.1 Variance index scoring system (VI scoring system)

The element of VI scoring system compose of 1) Designated value (DV), 2) Chosen coefficient of variation (CCV), 3) Variance index score (VIS), 4) Bias index score (BIS). The VI is an expression of the relationship between the laboratory's coefficient of variation and the coefficient of variation of the technique for the analyze which in some instance is called CCV. The CCV is not an actual value but it is an arbitrary scaling factor selected to represent the current state-of-the-art at that time and to produce various variance index of a similar magnitude for all analyses. The DV is the trimmed geometric mean. The variance index reveals the degree of deviation from the designated value. It is calculated from the following formula:

$$VI = \frac{(\text{result from participant} - \text{designated value})}{\text{designated value}} \times \frac{10000}{CCV}$$

For values of VI less than 400, VIS equal VI. The maximum VIS is 400. The BIS is identical to the VIS but retaining the sign; a result higher than the designated value will give positive BIS, whilst a lower result will give a negative BIS. In addition, they have Mean running BIS (MRBIS), Mean running VIS (MRVIS), Overall mean running VIS (OMRVIS), Standard deviation BIS (SDBIS). The MRBIS and MRVIS is a view of each analytes in each trial, but OMRVIS is a view of all anlytes all trials. For interpretation of the VI scoring system, the good performance is expected when the VI less than 50, it indicates that the value is closed to the method mean. The VI value of greater than 200 but not exceed 400 is needed to consider for correcting action (61).

3.4.2 Standard deviation index scoring system (SDI scoring system)

This type of scoring system usually used in quantitative hematology scheme. In addition, it is used in participant evaluation in PT in US. It is the calculation of a deviation index to indicate the difference between the individual results and SD. The SDI was determined using the following calculation:

$$SDI = \frac{\text{(participant data – peer group mean or median(after removing outliers))}}{\text{peer group SD}}$$

For interpretation of SDI scoring system. The laboratory who score less than 0.5 SDI have excellent performance. In contrast, if the result more than 3.0 SDI , it is considered as unacceptable performance. In addition, there are Overall standard deviation index (OSDI) and Overall mean standard deviation index (OMSDI) that indicate the SDI of all analytes in trial and all analytes in all trial respectively. The SDI scoring system can be modified in many ways, i.e. the peer group SD was substituted by e, where e is a limit of acceptability factor multiplied by reported result, or peer group SD was substituted by peer group mean multiplied by 100, then the result are compared with fixed criteria specified by CLIA. The results falling within the acceptable range are satisfactory (62). In PT program, to review an overall performance of five challenges per analyte, the percent of AD is calculated as follows:

If individual's result for an analyte challenge is more than target value:

$$\%AD = \frac{\text{(Individual laboratory's result – target value)}}{\text{(UL – target value)}} \times 100$$

If individual's result for an analyte challenge is less than target value:

$$\%AD = \frac{\text{(Individual laboratory's result – target value)}}{\text{(target value – LL)}} \times 100$$

where UL is upper limit deviated from target value , LL is lower limit deviated from target value. As long as the %AD for an individual laboratory's results are within the ± 100% limits of the %AD scale, there are acceptable for passing PT (63). Another way to estimate the chance to pass PT program is that if SD of IQC in their lab less than allowable error divided by 4. It is likely that laboratory is acceptable for passing PT program.

3.4.3 ABC scoring system

This type of scoring system only seen in UK NEQAS. UK NEQAS claim that this is a new scoring system to promote a harmonization scoring system. Confusing, it is seen in performance evaluation of UK scheme for peptide hormone

since 1988. The element of this scoring system compose of 1) All laboratory trimmed mean (ALTM) that is the geometric mean after 5% lowest and 5% highest removed, the ALTM sometimes modified as Method laboratory trimmed mean (MLTM), Group laboratory trimmed mean (GLTM). 2) Within-sample, between-laboratory agreement that is estimated as the geometric coefficient of variation (GCV) of the results used in calculating the ALTM, 3) Cumulative laboratory bias (BIAS) that is the geometric mean of the ratios of the laboratory result to the ALTM in the period of time. It is expressed as a percentage difference from 100, 4) The cumulative laboratory variability of the bias (VAR) that is the GCV of the ratios of the laboratory result to the ALTM. VAR describes the consistency of the laboratory's deviation from the ALTM; it reflects intra-and inter-assay precision. For interpretation of BIAS and VAR cumulative performance data, if the assay is low BIAS and low VAR, it can be interpreted that the assay is precise and giving results close to the target value. If the assay is low BIAS but high VAR, it indicate that there is wide scatter of bias on individual specimens. The high BIAS but low VAR indicated that the assay is clearly biased relative to the target value Common cause of this are errors in standardization. The acceptable of cumulative BIAS and VAR is 10-20% (64).

3.4.4 Misclassification index scoring system (MIS scoring system)

In semi-quantitative and qualitative tests, it is generally reported as titer or positive/negative. The scoring system for this is to use the MIS. The MIS system gives an indication of the number of instances where a laboratory has returned a qualitative response which is at variance with the designated result for the specimen. The designated result or the designated response can be derived from at least three mean i.e. preset by organizer in the light of the clinical information available or set by a panel of "expert' laboratories, and these may be achieved prior to distribution of the specimen, or define by consensus of the returned results among the participants with each scheme but is usually 80%. The MIS is the number of misclassifications by a particular laboratory during a defined period of time. In addition, there are Overall misclassification index score (OMIS) and Overall mean misclassification index score (OMMIS). The OMIS is consider all analytes each trial, but OMMIS is a ratio of the overall misclassifications to the total response in period of time. There are two types

of MIS scoring system; credit scoring system and penalty scoring system. For example, UK scheme for virology used credit scoring system, the score ratings on the scale 2, 1, 0, -1. If participant report fully correct, they get score 2. If participant report partly correct, incorrect but the results reported is not serious for clinical interpretation, and wrong report which serious significance, they get score 1, 0, and –1 respectively. The laboratory which get more score having excellent performance than that of less one; WEQAS qualitative scheme in UK used penalty system, the score are rating on opposite_ 3, 2, 1, 0. If the participant report fully correct, they get the lowest score_0. The laboratory which get less score having excellent performance than that of more one. An interpretation of MIS score depend on number of users or number of distribution i.e. number of distribution of 24, if OMIS more than 3, it is considered poor performance, and if more than 3 on three consecutive distribution, it indicates persistent poor performance (56,59,65)

3.5 Type of EQA

The EQA system can be distinguish as 1) proficiency testing, 2) “traditional” EQA scheme, 3) “educational” EQA scheme. Among these, the scheme design and criteria for acceptable performance are varies.

3.5.1 Proficiency testing

The term “PT” is generally used in America. PT programs have to respect current analytical performance and have wide acceptability limits, so it is non-stimulate and improvement of laboratory above that limit. In US, the system of PT is very complex by having many PT providers; The CAP and the American Association of Bioanalysts are the two largest providers of PT programs in US (5). However, there are state PT providers i.e. New York state PT program, State of Ohio. Historically, PT has been an education process, but now is regulatory and failure has serious penalties. Each laboratory must produce correct results on four of five specimens for each analyte and score overall at least 80% for three consecutive challenge. If more than two incorrect results are produced, the laboratory is considered “on probation”. If a laboratory has two or more incorrect results for any analyte or an overall score less than 80% on two or three consecutive surveys. That laboratory is classified as

“suspended’ and must cease testing all analytes until it is reinstated (66). There is an exception in ABO/Rh testing and antibody compatibility testing, for which acceptable performance constitute a perfect score (5/5 = 100%), because those test error can be life threatening, there is no acceptable limit of error for these tests. Only laboratories performs moderate and high-complexity tests classified by CDC are required to participate in PT program for accreditation and licensing. Successful participation in PT is require by several US Institutions such as the Health Care Finance Administration (HCFA), Medicare, Medicaid, the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO), the College of American Pathologists (CAP), and the Commission of Office Laboratory Accreditation (COLA). Each of them is accredited bodies have their own checklists. Their own checklist based on the federal regulations Clinical Laboratory Improvement Act (CLIA)’ 88. The function of each of organization is different i.e. CAP is a major accredited body than JCAHO because laboratories that are accredited by the CAP do not required to accredited by JCAHO. With exception in US, the only EQA in Germany conducted under legal constraintments laid down in the “Richtlinien der Bundesarztekammer” (RILIBAK) classiffed as a PT program (67).

3.5.2 Traditional EQA scheme

In a traditional EQA approach, a survey is run and afterwards the organizer tries to draw conclusions. It is a concept of EQA in the past or EQA system in third world countries. This type of EQA can be derived into voluntary and mandatory scheme. The voluntary scheme mostly focus on clinical outcome and education, but the mandatory schemes usually lined with laboratory license. The strengths of traditional EQA scheme are reduces punitive atmosphere which encourages discussion about the technical needs for new equipment and method, assesses staff competency and assists in improving staff confidence, improves communication with clinicians, improves the quality of testing, which ultimately improves patient outcomes. The weaknesses of traditional EQA scheme are increased costs for testing and evaluation that may be difficult to obtain and requests validated high quality sample, not government support, and laboratory may not follow up (68).

3.5.3 Educational EQA scheme

When EQA scheme is growing, Effort has been made to improve the shortcoming of traditional EQA scheme. The scope of education EQA scheme is much larger than traditional EQA scheme such as assessment of the overall analytical quality, long-term follow-up, assessment of quality improvement, define the origin of problem and to find the appropriate remediation procedure. The scheme design of this type of EQA is stringent. There is a good plan before sending out the sample, for example, when the scheme need to assess the bias of methods, the organizer must provide native control material. When organizer need to evaluate the laboratory performance, the multiple target value setting is appropriate. In contrast, the single target setting is appropriate in method performance evaluation. An education EQA scheme is the system of EQA in Europe. UK NEQAS is a good example established since in the late 1960s. It provides valuable information on the internet that easily to access than those of other countries. The administration section of UK NEQAS is good design. It composes of three main bodies, the consortium, the steering committee and the advisory panels and joint working group. The consortium consists of the representative from the organizer of the UK NEQAS. They have a responsibility for maintaining the professional standards and characteristics of UK NEQAS. The steering committee are appointed by the department of health, chaired by an independent expert, and consisting of technical experts together clinical advisers and representatives of the department of health. The role of the steering committee is to advise the organizer on the overall operation of the scheme. The steering committee deals with general aspects of performance as it relates to state of the art, but it is not concerned with performance of the individual participants. That is the function of the advisory panel, who are professional groups that have executive responsibility for maintaining satisfactory standards of analytical and interpretative work in laboratories in the UK. If the problems relating to EQA schemes, including complaints from participating laboratories, which cannot be resolved by the appropriate organiser, steering committee, or National Quality Assurance Advisory Panels (NQAAP), will be referred to the chairman of the Joint Working Group (JWG) who comprises representatives of the 12 professional bodies associated with laboratory medicine (69).

3.6 EQA scheme in Thailand

The first EQA scheme was started in October 1980 under the sponsorship of the WHO and with the assistance of Professor TP. Whitehead. Lyophilized control material for the scheme has been provided form the WHO collaborating center for research in clinical chemistry based at the Wolfson Research Laboratories in Birmingham, England, but the local distribution is undertaken by staff of the Institute of Health Research in Chulalongkorn University, Bangkok. Laboratory performance is assessed by the use of the VIS. Now, there are two mains NEQAS in Thailand, One is established by Department of Medical Sciences (DMSc). Currently, there are six NEQAS for laboratory medicine, clinical chemistry, clinical microbiology, clinical hematology, clinical microscopy, clinical immunology and blood banking. All proficiency testing schemes are voluntary and free of charge to enable laboratories to participate in any scheme at any time as needed (70,71). Another one is EQA established by Faculty of Medical Technology, Mahidol University since 1987 in clinical chemistry, EQAC for short. The lyophilized control material used in the scheme was in-house prepared and analyzed for 23 routine biochemical analytes. A blind lyophilized control serum was monthly-cycle distributed by post together with appropriate report form. The proficiency statistic of each participant's laboratory was calculated using VI scoring system (72).

EQA in clinical hormone, EQAH for short, was established in early 2000. Lyophilized control serum was in house prepared were dispatched to participant together with report form. The EQAH organiser dispatched specimens 4 time/year, 3 blind levels for testing a T3 (total T3), T4 (total T4), FT4 (free T4) and TSH. The CCV of all tests is 15%. Cotivongsa P et al (2003) reported ,during the year of the 10 trials experience, the inter-laboratory VIS mean covered ranges of T3, T4, FT4 and TSH by 52-70, 37-60, 47-62, and 44-64 respectively, and the percentage of laboratory participants that achieved good performance (less than 100 VIS) of T3, T4, FT4, and TSH were 77-90%, 81-96%, 84-93% and 83-93%, respectively (73). In the year 2004, FT3 was include in this scheme.

EQA in microscopy (EQAM) was also established in 2000. There are four subschemes; B:EQAM, H:EQAM, U:EQAM, C:EQAM. The B:EQAM operate the use of in-house prepared partially stabilized whole blood for evaluate the cell count

laboratory performance. H:EQAM use 2 stained slide for blood smears examination. C:EQAM use 2 photograph for blood identification, and U:EQAM use 1 urine mounted slide for microscopic examination. The evaluation criteria of B:EQAM is to use the SDI score. According to SDI score, the laboratory result will be graded by comparing with all methods and within groups. The evaluation criteria of H:EQAM is to use the correct "S" or incorrect", "Need action or NA" answers judged by expert referees or 50% consensus answers from all participants by %CV less than 30. If laboratory result fall within referee or participant group range, the result will be considered as correct and the result will be graded. For B:EQAM, the evaluation criteria as same as H:EQAM but the use of consensus answer is 80%. There may be two correct answer from those referees and participants if the referee answer do not match the consensus answer. For U:EQAM, MIS was introduced to access laboratory performance. The evaluation criteria the criteria quite the same as H:EQAM, and there may be two correct answer as the same as H:EQAM. In hematology scheme, participant must be participate all sub-schemes because the performance evaluation will be concerned each other (74).

EQA in immunology (EQAI) was established in 2001. Now, there are only two subschemes, syphilis serology and Hepatitis B virus serology. EQAI organiser was in house prepared liquid form of control material by using Bronidox as an antimicrobial agent in these 2 subschemes. Control material were dispatched 4 trial/year. MIS was selected to evaluated in qualitative test result, while SDI was used for quantitative test result. Sarntivijai S et al (2003) reported, after 4 years implemented, that 97% of the laboratories participated in syphilis serology and 100% for HBV serology scheme are in an acceptable range of assessment (75).

3.7 EQA scheme in Tumor marker

The first EQA in tumor marker started at the beginning of 1980s (76). With an increasing role of tumor markers in oncology, Now, there are many tumor markers schemes in the world i.e. UK (64), USA (77), Japan (78), Finland (79), Czech Republic (80), German (81), Italy (12), RIQAS (55), RCPA (82), and Korea (83). Each scheme provide different in how deep in detail. Unfortunately, EQA in German provide in their own language (81). In Korea, it has been started in 1995. Up to now,

it limited only four tumor marker; AFP, CEA, PSA, hCG. In Czech Republic, It is organized name SEKK. It was performed in collaboration with the Czech Society of Nuclear Medicine and the Czech Society of Clinical Biochemistry. It dispatched lyophilized human serum 2, two samples each survey. The quality of laboratory observed by Z-score. If $|Z| < 1$, it shows excellent result, no comment. If $1 < |Z| < 2$, it shows good, acceptable result. If $2 < |Z| < 3$, it shows doubtful result, method check is recommended. If $|Z| > 3$, it shows severe error in the determination. It is also show the standard deviation, coefficient of variation and percentiles (16th and 84th) are given only in groups the frequency of which is 5 at least (80). In Japan, there is reported in proceedings of the 2nd Colloquium : Asian network for clinical laboratory standardization and harmonization (ANCLS) (78). In Finland, It is operate namely Labquality. It provides 2 liquid sera; 3 ml per vial. Each of them is dispatched 3 times a year: February, May, September (79). In Italy, It is manage under Consiglio Nazionale delle Ricerch (CNR). It is limit only AFP, CEA, hCG and dispatch ten times a year (12). In UK, tumor markers schemes consist of AFP, CEA, and hCG seen in peptide hormones and related substances scheme, meanwhile, CA antigens, PSA are in immunology & immunochemistry scheme. For tumor markers-AFP, CEA, PSA, hCG, the material distributed is liquid human serum preserved with 0.5% v/v Kathon CG-ICP II solution that dispatch 12 times per year and 5 samples per distribution, and the volume provided is 0.5-1.0 ml per specimen, depending on the analyte. Organiser provides a data evaluation by using ABC of EQA scoring system. Because reference methods are unavailable, UK NEQAS attempt to used ALTM as a target value agreement with expected values comfirming by recovery, stability, linearity experiment. However, in hCG, the grouped-method mean are used as target value. For tumor markers-CA antigens, PSA, Organiser evaluate laboratory performance by VI scoring. The CCV for CA125, CA15-3, CA19-9 is 10%, 12.5%, 12.5% respectively. The material distributed in CA antigens is human serum-normal and pathological which add the purified tumor antigens to normal human serum that dispatch 12 times per year and 1 samples per distribution for PSA and dispatch 6 times per year and 2 samples per distribution for CA antigens (64). For tumor markers schemes in US, there are many PT program provided i.e. American Proficiency Institute-state of Washington public health EQA (84), Accutest Co Ltd (85). In Accutest Co Ltd, it is

available in special chemistry for hCG, the price for participation are 175 US dollar/year ; and in tumor marker scheme for AFP, CEA, CA 125, CA 15-3, CA 19-9, tPSA, fPSA and PSA free/total ratio, the price for participation are 295 US dollar/year. It provides 3 shipments/2 samples and used liquid human form. For tumor markers survey provided by CAP, the results are evaluated based upon a range of acceptability that range is determined using a target value and a limit and it is peer group mean. The peer group mean ± 3SD are used as evaluation criteria in tumor markers schemes. It fewer than 10 laboratories have reported results, a peer group mean may not be established. Instead of that, the median is established (82). In addition, there are several commercial companies organize an EQA scheme coupled to the purchase of control materials by clinical laboratories. RIQAS immunoassay program was established in 1993 . Currently, RIQAS is running a free-of-charge pilot study of CA15-3. RIQAS used human based-lyophilized sample, 5 ml per vial. It runs the tumor markers program two cycles per year. Each cycle consists of a pack of 12 numbered samples. For statistic analysis, the results were used to calculate the mean, SD, and %CV. Then Chauvenet's criterian that is the SD is multiplied by special factor depending on the number of results used to calculate the mean, was carried out to exclude results which lie outside the criteria . The remaining results were used to calculate the mean, SD, %CV, chauvenet's ceteria again. If there is no further result excluded by Chauvenet's criterion, then a 95^{th} percentile exclusion was performed. If there are outlier from 95^{th}, the 95^{th} exclusion removes any results greater or lesser limit. the remaining results were used to calculate, the mean, SD, and %CV again. If there is the result fall outside the mean ±1.96SD range, these are excluded and the remaining results are used to calculate the mean, SD and %CV presented on the participant's report. In addition, it also provided graphic bar graph, Levey-Jennings chart, Target score chart (TS chart) (55). RCPA Quality assurance programs Pty Ltd have organized since 1982. Tumor markers scheme are currently available, two scheme cycles are run per year: Each scheme cycle is made up of a set of twelve lyophilized unknown samples, whereby the samples within a cycle are run as pairs, at regularly scheduled interval over a six month period. To assessment of performance, the results of participants are compared to target values. The target value is determined by laboratories selected by program organizers which use the best available methods.

It also combine the target value and allowable limit of performance that based on patients needs rather than the state of the art. For tumor marker, the acceptable range are following : AFP ± 5 in case of ≤ 25 kIU/L or ± 20% in case of >25 kIU/L, CEA ± 2.0 in case of ≤ 10 μg/L or ± 20% in case of >10 μg/L, PSA ± 1.5 in case of ≤ 10.0 μg/L or ± 15% in case of >10 μg/L, CA125 ± 10 in case of ≤ 50 kU/L or ± 20% in case of >50 kU/L, CA15-3, CA19-9 and hCG ± 3 in case of ≤ 20 kU/L or ± 15% in case of >20 kU/L (82).

4. Tumor markers

To study about tumor markers, something needed to keep in mind is that there are many controversies about tumor marker , for example, the tumor markers classification. Some authors state that AFP, CEA, PSA, CA125, CA15-3 and CA19-9 is the oncofetal antigen, hCG is a placental protein, but some stated that the oncofetal antigen is only AFP and CEA, for PSA, it is considered as enzyme, for CA125, CA15-3, it is a carbohydrate markers, and for CA19-9, it is a blood group antigen (4,86). Although there are many tumor markers; however, in our survey study, the tumor markers conducted limited only serological marker; AFP, CEA, PSA, CA125, CA15-3, CA19-9 and β-hCG. Each of tumor marker associated with different malignant diseases in spite of less specificity and sensitivity i.e. for AFP, it is often elevated in primary hepatocellular carcinoma. for CEA, elevated in colorectal carcinoma, for PSA, elevated in prostate cancer, for CA125, elevated in ovarian carcinoma, for CA15-3, elevated in breast cancer, for CA19-9, elevated in pancreatic and gastric carcinoma, and for hCG elevated in choriocarcinoma, but various type of benign and malignancy condition can result in elevation of these tumor marker; so there are no tumor markers assay approved by the Food and Drug Administration (FDA) for routine clinical use, it is only for investigational use only (87,88). Because the ease of drawing blood and require only noninvasive technique, the tumor marker testing still use for screening, diagnosis, prognosis, monitoring response to therapy and detection of early recurrence of cancer. Each of tumor marker has different role, it depends on many parameter such as epidemiological factor, analytical sensitivity, analytical specificity, predictive value and reference value. For example, actually only AFP, CEA, PSA, CA15-3, CA19-9, and β-hCG, they can not be use for

screening the general symptom-free population. It can be used for screening in special case, for example, AFP can use for screening hepatocellular cancer in China because the high incidence of liver cancer in that area. Another example is that PSA in combination with a digital rectal examination (DRE), the use of PSA in screening prostate cancer in men about age 50 is feasible because the high incidence. And there is a use of CA125 for ovarian cancer screening, however, it is still in the process of investigation. For diagnosis role, because there is no absolute clear cut-off between healthy and cancer group, so there is no tumor marker having 100% sensitivity and specificity. The adjustment is required. Emphasize on sensitivity is desired in the disease that is serious and should not be missed, can be treatable, and the false-positive result do not lead to serious physical, psychological, or economic stress to the patient, but emphasize on specificity is desired in the disease that is serious but is not treatable or curable, and false-positive results can lead to serious psychological or economic stress to the patient (89). The use of CEA, CA125, CA15-3 can not use for early diagnosis purpose, because an elevation are related to tumor burden. , the use of multiple markers is one approach that can improve the diagnostic power of tumor marker. An example of this approach is to combined use of AFP and hCG helpful in the differential diagnosis of various germ cell tumors. Another example for PSA, the use of serum PSA, PSA velocity, and PSA density, and age-adjusted reference intervals can improve the ability of PSA testing to detect early prostate cancer. However, be cautious with this approach, because it create unnecessary cost, for example, the use of CEA combine with CA15-3 does not improve the sensitivity to detect adenocarcinoma of the breast and combine measurement of CEA and CA19-9 does not improve the effectiveness of management of pancreatic carcinoma because it is a parallel each other. So it should be kept in mind that only the complementary marker should be selected, for example, the use of CA15-3 combined CA125 can increase the specificity of the CA125 for distinguishing malignant of ovarian from benign disease. With exception of CA15-3, all of tumor marker can be used for prognosis because the degree of elevation correlates with tumor stage and size. Elevated AFP level (>10 μg/l), as well as serum bilirubin level greater than 2 mg/dl, are associated with shorter survival times. A prognosis of CA125, in women in whom the fall of serum CA125 after therapy followed a half-life of five days, prognosis was

much better than in women in whom it did not. The most useful applications of tumor markers are monitoring treatment. All of tumor markers reflects well the success of surgery or the efficacy of chemotherapy, with an exception CA15-3 because declining levels do not always occur in patients undergoing successful therapy. To monitor the efficacy of treatment, serial measurement in specific time interval are required. CEA monitor should be done at the start of treatment and then every 2 to 3 months thereafter. The change 25% to 35% has been termed significant. For PSA, the PSA levels should be measured every 3 months after surgery, every 4 months in the second year, and every 6 months thereafter. The significant change should be ± 30%. There are many factors effect such as tumor markers half-life and pathological factor in patient. If there is an effectiveness of cancer therapy, the marker should be decreased according to their half-fife. Each of tumor marker has different half-life, for AFP, the half-life is 5 days, for CEA, the half-life is varies between 2-8 days, for PSA, the half-life is 3 to 4 days, for CA125, the half-life is 4.8 days, for CA15-3 and CA19-9, the half-life is not assigned, for β-hCG, the half-life is 12 to 20 hours. An example of the use of half-life of serum PSA is that it will take 30 days for a serum PSA at 50 ng/ml to drop to an undetectable range following successful surgery; however, some disease, for example, if patient suffer from renal or liver disease, even though the therapy is effectiveness; but serum CEA level is not reaching to half of the initial level because there is an impairment to remove tumor markers from the blood circulation due to liver disease. The second most important role of tumor markers role is to detection of recurrence. All of tumor marker can fulfills this role, but there exits the difference about the time to ensure that there is no recurrence, and how many percent difference can be considered as a significant difference. For CEA, it has been suggested that the lead time from CEA elevation to clinical recurrence is 5 months. For PSA, the time between PSA concentration elevation and clinical recurrence is between 1 and 5 years. For CA125, the level above 35 U/ml are indicative of tumor recurrence. For CA19-9, elevated levels can indicate recurrence 1 to 7 months before a recurrence is detect by clinical finding.

For the method of analysis, it was not until the invention of the radioimmunoassay that the term tumor marker introduced and became a part of the everyday laboratory vocabulary. From now on, the use of polyclonal antibodies , and

at present, the development of hybridoma technology to produce monoclonal antibody lead to develop automated immunoassays to measure tumor marker. Now, labeled immunoassay, available commercially, are used in tumor marker analysis. Most of them use nonisotopic labels, such as enzyme, fluorescent, chemiluminescence, and immunochromatography in test kit system, especially an assay sandwich format. Each manufacturer invents specific antibody to detect different epitope on tumor antigen. For AFP, CEA, PSA and β-hCG, there are none of manufacturer states the specific epitope of tumor antigen; they state only that kind of anti-tumor antigen For CA125, all of them use anti-OC125 as a capture and conjugated antibody. For CA19-9, all of them use anti-1116-NS-19-9 as a capture and conjugated antibody. For hCG, its structure consists of two dissimilar α- and β-subunits. the assay designed for total β-hCG, meaning both of intact and free β-subunits are measure in unison. They use monoclonal anti-β-hCG as a capture and polyclonal anti-β-hCG as a conjugated antibody. Using anti for free α- and β-subunits, it detects only the intact of hCG. It is disadvantage because most individuals with germ cell tumor produce both free β-subunits and intact molecules. For CA15-3 , there are reported about the difference in antibody defined antigen for CA15-3, most of them use anti-115D8 as capture and use anti-DF3 as conjugated antibody, however, DPC Immulite 2000 uses anti-Ma695 as capture and use anti-Ma552 as conjugated antibody; and Centaur™ uses anti-B27.29 as a capture and conjugated antibody (90). With the difference manufacturers, the assay format are also different. Some assay system needs to separate bound form from free components. The immunoassay in which no separation step is necessary called homogeneous immunoassay i.e. the measurement of CA125 and CEA in Cobas core modal . For the immunoassay which require separation step called heterogeneous immunoassay, most of assay available in market are heterogeneous immunoassay. Once the reaction between antigen and antibody has taken place, their need to be enhance analytical measuring system by using labeled sites; Each manufacturer use different labeled. For enzyme labeled commercial, Access, AxSym, use alkaline phosphatase, while Cobas core, Vitros Eci, test kit use horseradish peroxidase. For labeled commercial chemiluminescence, Elecsys, modular E170™, use ruthenium complex (ruthenium(II)-tris(bipyridyl) ($Ru(bpy)32^{+}$. When patient antigen is incubated

with solid-phase antibody, then, conjugated-labeled antibody is added, which combines with additional determinant sites on the bound antigen. Afterthat, substrate for conjugated-labeled antibody is add; there exists many type of substrate i.e. AxSym use 4-Methylumbelliferyl phosphate (MUP). For Elecsys, Modular E170™ use tripropylamine (TPA), for Access, use Dioxetane-P, for Cobas core and assay kit use tetramethylbenzidine (TMB), in Vitros Eci, the substrate is luminol derivative and a peracid salt. In Immulite, the substrate is an adamantyl dioxetane phosphate (91-96). The drawback of immunometric method is that, it is always interfered from HAMA in the serum of cancer patient who was undergone immunoscintigraphy with monoclonal mouse antibody. The another drawback is the effect of hook effect. This effects tend to give a falsely low value when the tumor marker concentration in the specimen rises above a certain highly elevated concentration (97). In labororatory point of view, there is no need of patient preparation, serum is prefered to use as an specimen. The specimen can be storage 2-8° C up to 24 hours and –20 ° C in case of storage time longer than 24 hours. The reference range of tumor markers are in controversy; however, when ordering a tumor marker testing, it should never rely on the result of a single test because it can found the transient elevations. Ordering serial testing can help detect falsely elevated level due to transient elevations. When ordering serial testing, be certain to order every test from the same laboratory using the same assay kit because the different assay and even the same assay with different lots of reagent may produce different results. The reason for such differences are due to changes in assay calibration, production lot variation, assay reaction time, reagent matrices, assay sensitivity, and imprecision. An example of different antibody specificities PSA testing, some assays are classified as eqimolar because both antibodies binds to free and complexed PSA equally, some assay are nonequimolar because both antibodies binds to free or complexed differently. Another example is total β-hCG, if the binding affinity of intact hCG and β-hCG are not equally, they also produced difference value even they are a same total β-hCG assay. To order tumor marker testing, the timing of blood sampling is usually not critical because no strong evidence of diurnal variation for most tumor markers. The within-patient factor should be considered instead because it might lead to misdiagnosis, for example, during pregnancy, maternal AFP level can be increased, serum CA125 can be elevated in menstrual cycle, and in

healthy population who heavy smoker, the reference range can be up to 10 ng/ml for CEA, CA19-9 is only found in the serum of individuals who secrete Lewis antigen, and serum PSA has been reported to decrease by 18% after the patient has been hospitalized for 24 hours. Now, the general requirement of tumor marker assay is that the intra-assay variance should be <5%, inter-assay variance <10%, the specificity > 95%, and the sensitivity >50% (97).

CHAPTER 4
MATERIALS AND METHODS

1. Materials

1.1 Apparatus

Axsym, Automated immonuassay analyzer Cat No. 10246-96 Abbott company, Germany.

Computer Model Pentium II Processor Intel-M-Mx™ Technology, 128 MB Ram, 6.0 GB Harddisk, Softtech company, Thailand

Deep-freeze –86 °C, Cat. No. S/N 85945-82, Forma Scienatific Incop.

Filter 20 μm pore size, AP 20 Cat no. 07500 Dia 75 mm, Millipore, USA.

Filter membrane 0.45 μm pore size, AW06, Cat.no. 090 00 Dia 90 mm, Millipore, USA.

Freeze dry/ SHELL FREEZE SYSTEM, FREEZE 6, Cat No. 7753511J, LABCONCO Corporation, USA.

Freezer –20 °C, Model FC-27, Sharp, Thailand.

Magnetic stirrer plate , Model MT2, Amicon, USA.

pH meter, Model 611, ORIAN RESEARCH, ENGLAND.

Pipette, Model 8100, Nichiryo Co.,LTD, Tokyo, JAPAN

Refrigerated centrifuge, high speed, Model J14C, Beckman, USA.

Rotator, Centrex Co., Thailand

Stainless steel filter holder, Millipore, USA.

Stopper 7x13 gray butyl, Cat. No. 224100-081, BIOMED company, Germany

Trip balance 2 kg-5 lb capacity, Model OHAUS, Marcareg, USA.

Vacuum Pump, Gilford, OH, USA.

Vial 3 ml, 7x13 mm mouth ID, Cat. No. 223684, BIOMED company, Germany.

250 ml centrifuge tubes Cat. No. 340198, Beckman, USA.

1.2 Chemical

Bronidox (propylene glycol and 5-bromo-5-nitro-1,3-dioxan, Henkel company, Germany.

1.3 Reagent

Axsym AFP reagent for detection of AFP, Cat No. 7A48 66-9117/R8, Abbott company, Germany.

Axsym CEA reagent for detection of CEA, Cat No. 7A47 69-3791/R7, Abbott company, Germany.

Axsym CA125 reagent for detection of CA125, Cat No. 3B41 34-0975/R5, Abbott company, Germany.

Axsym CA15-3 reagent for detection of CA15-3, Cat No. 3B42 69-0499/R3, Abbott company, Germany.

Axsym CA19-9 reagent for detection of CA19-9, Cat No. 7A50 66-9112/R4, Abbott company, Germany.

Axsym PSA reagent for detection of PSA, Cat No. 7A49 66-9951/R6, Abbott company, Germany.

Axsym β-hCG reagent for detection of β-hCG, Cat No. 7A59 66-4682/R13, Abbott company, Germany.

1.4 Miscellaneous

Broken-proof plastic bag

General glassware used in this study were from Pyres®, USA, Kartall , Milano, Italy and Witeg, Germany

Mailing envelops

Labeling stickers

1.5 Serum

Hepatitis B surface antigen (HBs Ag), Anti-HIV, Anti HBs Ag, Anti HBC non-reactive donating serum from side tube discarded from the National Thai Red Cross

was used as serum source of normal serum. Sera collected from National Institute of cancer was used for spiking . All sera were kept at -86° C freezer until used.

2. Methods

2.1 Questionnaire design

Questionnaire is designed in order to gather a necessity information from laboratories (98). It is held as secret only organizer known a secreted data. The confidential data is useful for organized scheme. The set of questionnaire, which prepared in Thai, was dispatched by surface mail to EQAC's participant- Community hospital, General hospital, Regional hospital, Medical center hospital and University hospital, Private clinical laboratories and laboratory belonging to Private hospital, that survey up on 12th December 2001. This was done on 31st October 2001 and asked to return the form within 1 month afterwards. The returned answers were analyzed for information that will be of useful for scheme establishment. The question are in series of laboratory name, laboratory director, address, telephone number, hospital name, amount of bed, to be under, the status of tumor marker testing and instrument, currently participation in EQA tumor marker scheme, interesting to join in EQAT schemes of The Faculty of Medical Technology, Mahidol University.

2.2 Control material preparation

Pooled sera from National Thai Red Cross were centrifuged at 2500g for 30 minutes with high-speed refrigerated centrifugation. Then, those sera were filtrated to remove a insoluble fibrin by filter 20 μm pore size with pressure from pump. Next, those sera were filtrated again by pre-filter 20 μm pore size incorporated together with the micro filter pore sizes 0.45 μm by using nitrogen negative pressure pump apparatus to minimize microorganism and clear. After that sera with known value of tumor marker from National Institute of cancer were added into pooled sera from National Thai Red Cross in order to obtain a desired concentration of tumor marker. Those of samples passed the process above are filled in each vial accurately 1 ml. Then, the samples are divided into two group, one is native liquid form, which added with 0.2% Bronidox, and the second group of the vials are lyophilized in the freeze

dry instrument. After all processes completed, the vials are capped immediately and aluminium closure rings placed above the rubber stoppers and compressed by a hand crimper, attached the labeling stricker which carry explicit information of the name of the EQAT manufacturing, batch number, the type of matrix and where appropriate the volume of distilled water to be added (99). Finally, control sera were analyzed 5 times to established target value. In order to saving cost, it is assumed that the target value of liquid form and lyophilized in Day 0 form are equal.

2.3 Selection of the appropriate preparation of EQA materials

This study covered the selection of an suitable form of EQA material i.e. native liquid serum preserved with 0.2% Bronidox versus lyophilized serum and the stability of various prepared EQA materials. Each form consists of two levels. Each form and level was divided in 2 groups. One group was kept in 4° C, another one was kept at room temperature. On testing day arrival, liquid form can be directly analyzed, but lyophilized control material was reconstituted with 1 ml distilled water and allowed to completed reconstituted.

For round trip mailing at ambient temperature, the lyophilized and native liquid form were sent by surface mail and asked to return samples to the Faculty of Medical Technology, Mahidol University. On the arrival day, the specimen were analyzed by Abbott AxSYM^{TM} (Abbott Labs., North Chicago, IL) (100).

2.4 Data analysis

The returned answers of the questionnaire were analyzed for tumor markers being performed in each type/size of laboratories, the EQA scheme membership status of the laboratory, and the requirement for EQA schemes in tumor marker tests by using descriptive statistic performed on SPSS software version 10.0 (SPSS Inc., Chicago, USA).

To evaluate the stability, and suitable form of control serum both of liquid and lyophilized form, commercial control sera ware analyzed in parallel with our control material to check Abbott AxSYM performance. The stability of control sera ware evaluated based on clinical significant changes concept. The Reference change value

(RCV) of each tumor marker is established to monitor changes in serial result as following;

$$RCV = 1.414 \times Z \times (CV_A^2 + CV_I^2)$$

Where Z is a standard normal deviated from mean of normal distribution, CV_A is a analytical variation during do the stability test, CV_I is within-subject biological variation.

For round trip mailing stability test, the difference of tumor markers measurement before dispatch and after dispatched are calculated and compare against RCV. If there is a deviation exceeds the RCV, the control material are considered as instability (7). The process flow diagram of this study was summarized in following

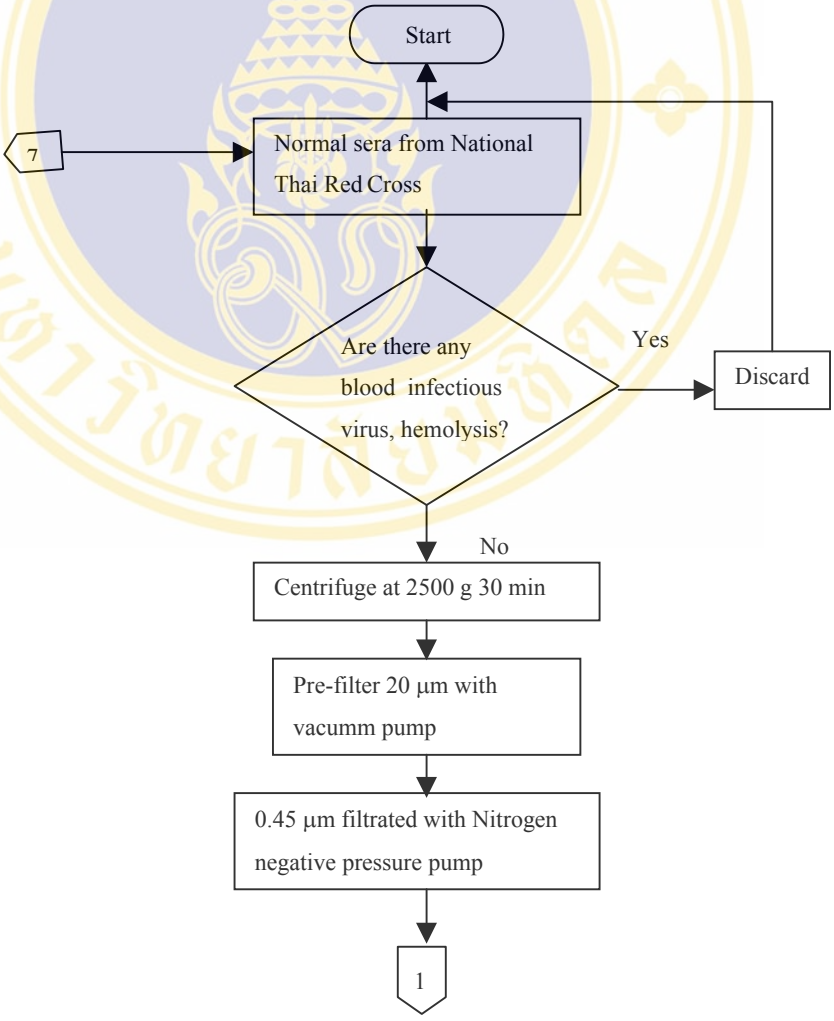

Figure 1A. Control material preparation and selection algorithm

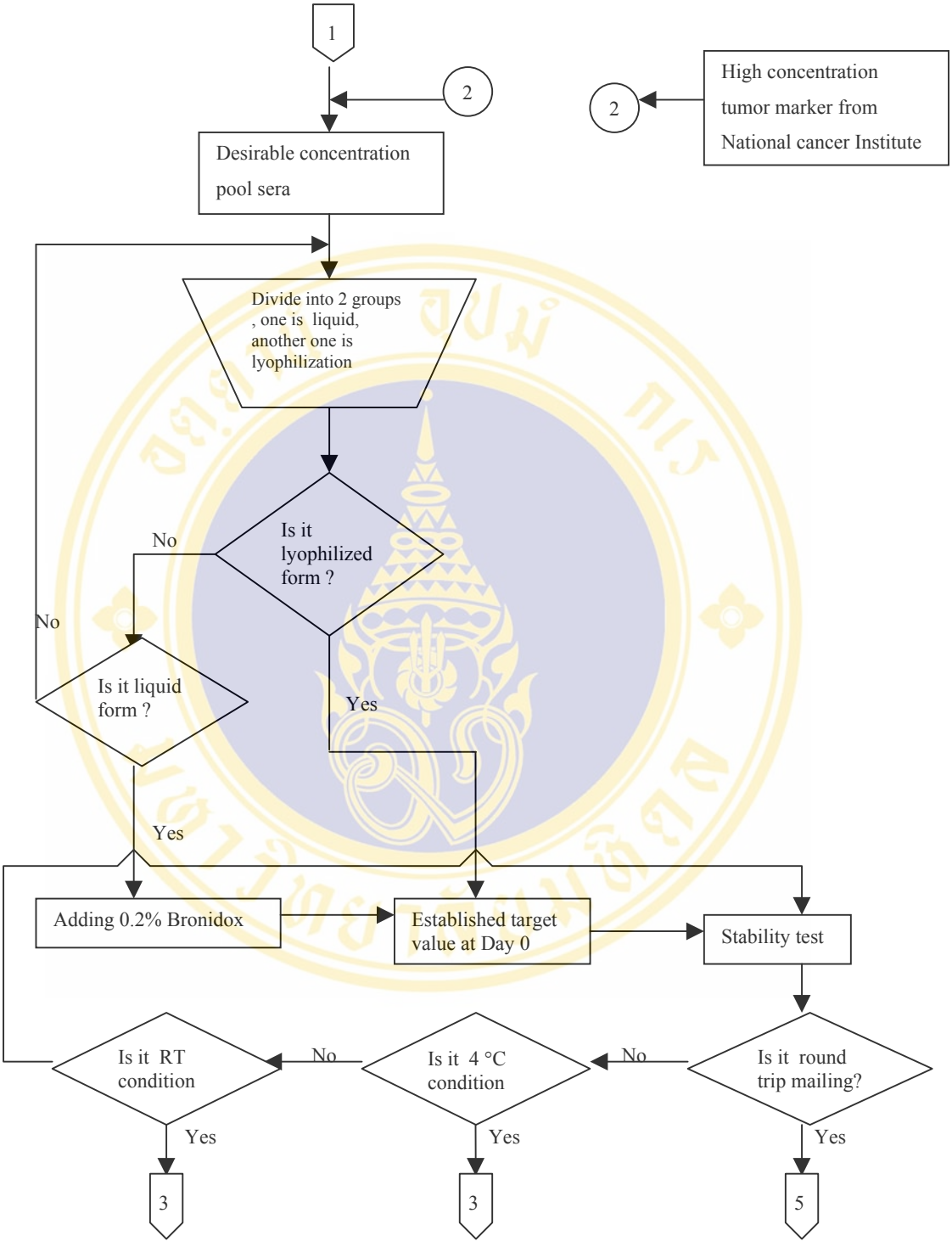

Figure 1B. Control material preparation and selection algorithm

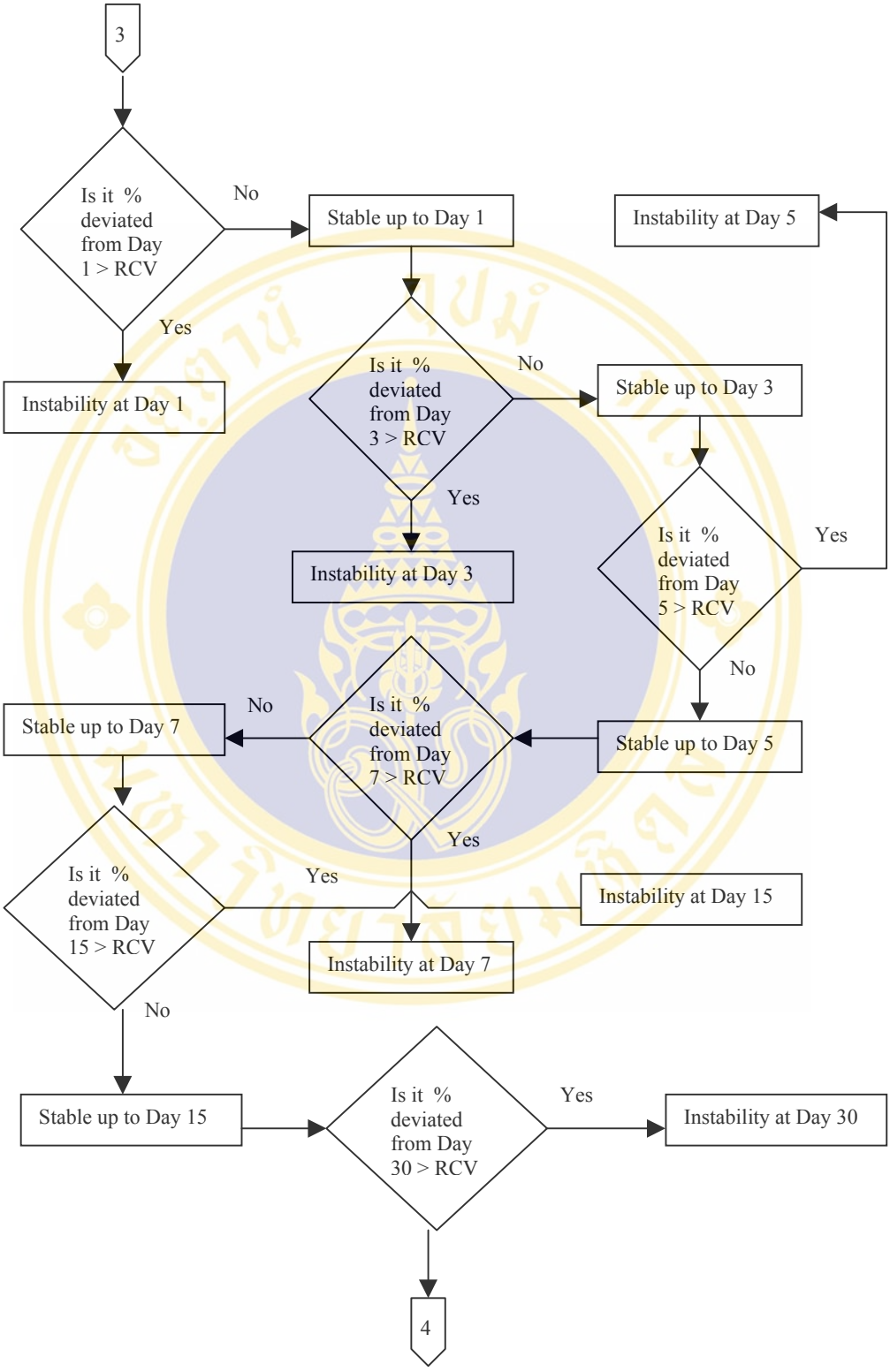

Figure 1C. Control material preparation and selection algorithm

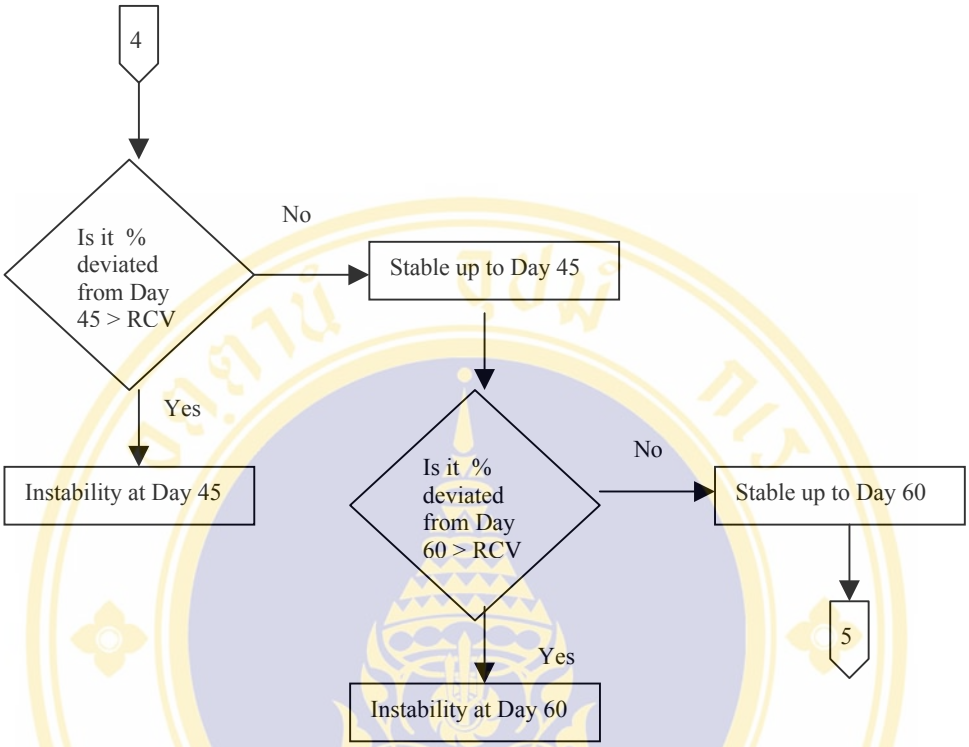

Figure 1D. Control material preparation and selection algorithm

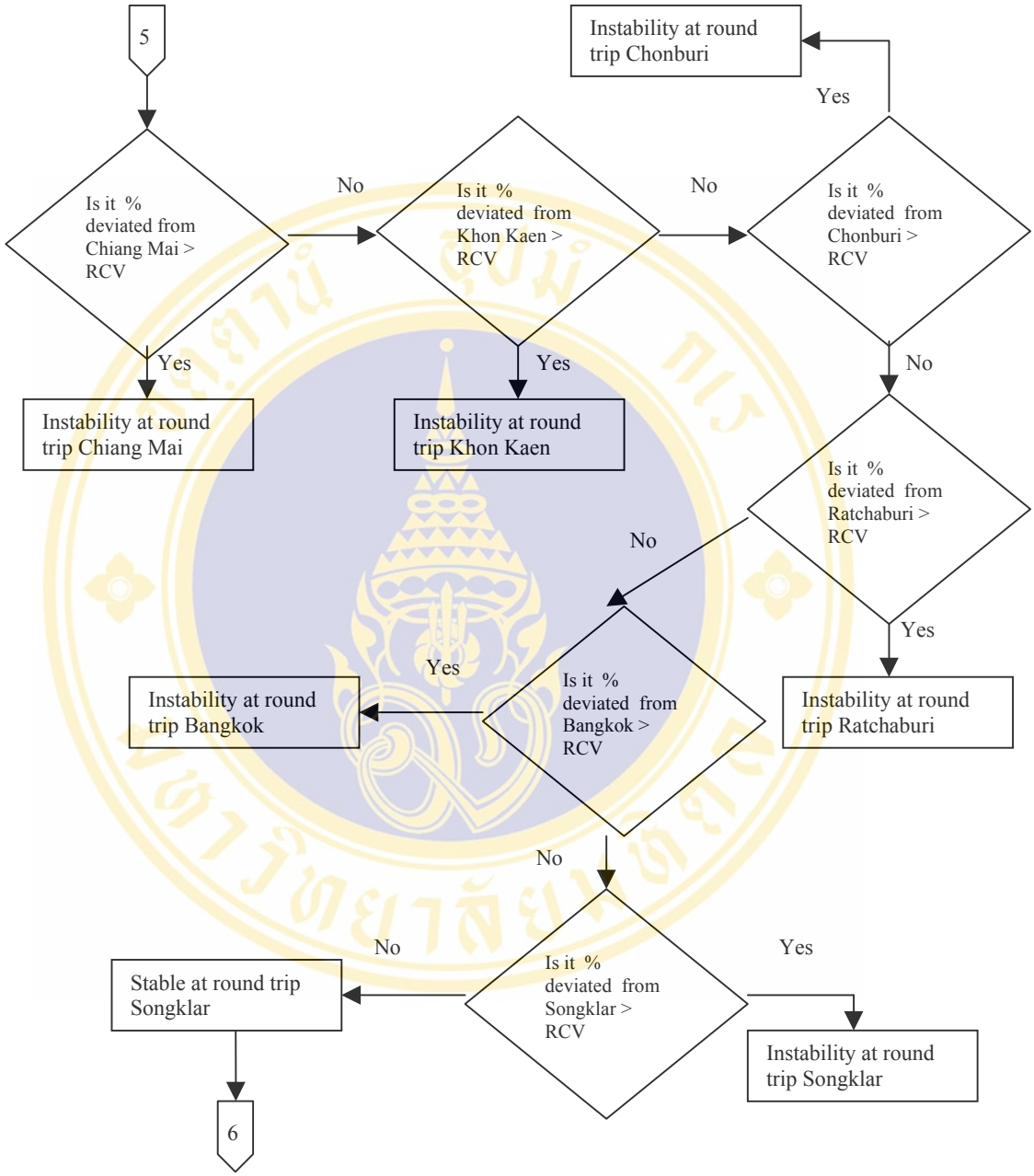

Figure 1E. Control material preparation and selection algorithm

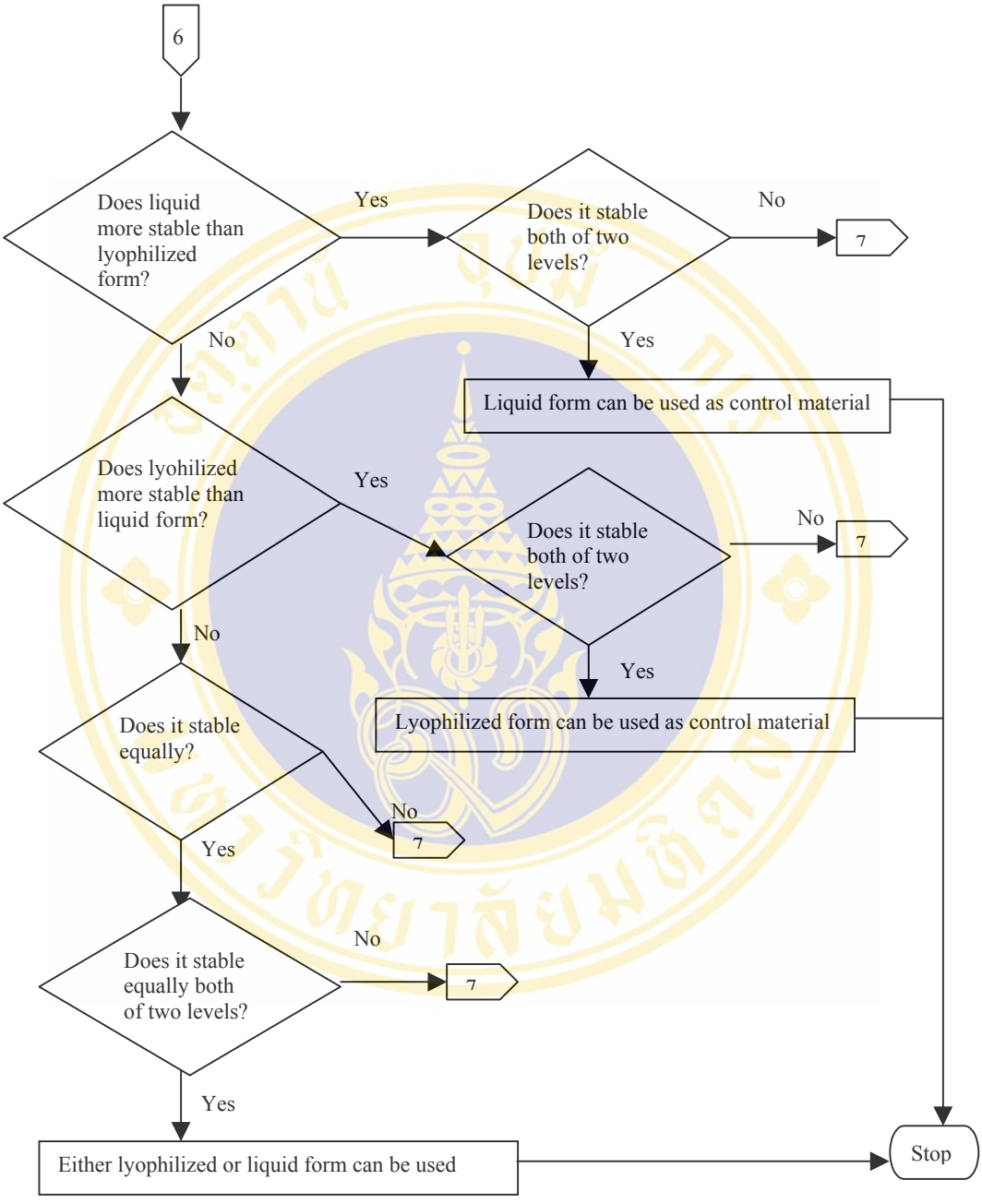

Figure 1F. Control material preparation and selection algorithm

2.5 External quality assessment scheme in tumor markers (EQAT) pilot project

2.5.1 Plan for EQAT pilot projects

Fifty five returned the form which indicate the intention to participate in these EQAT scheme as in the questionnaire identified. Each of participant is identify by code number and this was kept confidential. the EQAT scheme consist of AFP, CEA, PSA, CA125, CA15-3, CA19-9, and β-hCG. Control materials were plan to sent to participants 6 times per year; January, March, May, July, September, November. It consists of 2 specimens under different code number within the same trial. A volume of 1.0 ml of each serum was distributed into 3.0 ml rubber-capped vials and identification number labeling sticker was adhered. Eighty vials were prepared for each specimen. This number came from the number of participants plus 10 percent surplus. Before dispatched, these vials of samples were kept in refrigerator (2-4 °C). When the dispatch dated arrival, two samples were wrapped in a broken-proved plastic bag and tightly sealed. This specimen was put in an envelope and sent to each member at ambient temperature by ordinary surface mail of Post and Telegraph Department, Thailand. Delivery time took about 3-4 days. The specimen were sent together with the instruction form which provided general information of the control materials, instruction for treating and testing the control material, the report form which provided the information required from participant including the member code numbers, test performed, assay method, test results and signature and name of authorized person, and lastly the assessment report form which was prepared in order to inform the participants of their method used, and their reported result analysis.

2.5.2 Performance evaluation

This is done by program LOTUS 1-2-3 release 5. In each of tumor markers, the organizer is classified the method as different groups. The result analysis compose of 8 pages. The first page is an individual laboratory report. It consist of designated result for each sample (DV), SD, %CV BIS, VIS, within-lab VIS, between-lab VIS, the number in their group. The second and third page is all group and each group mean, SD, %CV and the number of each group. The fourth and fifth is grade report classified by instrument used. The sixth, seventh, and eight page is graphical report of

the Running BIS (RBIS), the Running Mean VIS (RMVIS) of each tumor marker within laboratory. The RBIS was derived from a BIS of the specimen each trial. The RMVIS is the cumulative VIS of all previous and recent trials. It would indicate the performance of a laboratory for that kind of test in a specific time period. The CCV of all tests is 15%. The performance indicator of the participant laboratories was granted as followed (72).

MVIS score ≤ 50	→	Excellent performance
MVIS score 51 - 100	→	Good performance
MVIS score 101 - 150	→	Medium performance
MVIS score 151 - 200	→	suspected performance
MVIS score > 200	→	need correction performance

After the last trial, the overall performance were evaluated. The mean of all laboratories MVIS were shown in graphical form. The number of participating laboratories in each categories of MVIS, excellence, very good, good, medium, need correction are tabulated. The mean of %CV of each tumor markers classified by method and by trial are calculated shown in descriptive and graphical form.

CHAPTER 5
RESULTS

1. Current status of tumor marker tests, and requirement for EQA schemes in tumor marker (EQAT) of laboratories in Thailand

The questionnaire was designed in Thai as shown in Figure 21A-21C in Appendix. To study the current status of EQA , the tumor marker tests performed in the laboratory, and the need to participate in EQA tumor marker scheme, the set of questionnaire was sent to 400 laboratories on 31th October 2001 and 129 (32.2%) returned the forms as shown in Table 1. There are 70 out of 129 laboratories performed tumor marker testing. It could be summarized that AFP, CEA, β-hCG were mostly done in provinces, government, 120 – 500 beds size hospital. tPSA, CA125, CA15-3 and CA19-9 were mostly done in Bangkok, private, 120 – 500 beds size hospital. In contrast, fPSA mostly done in provinces, private, 120 –500 beds size hospital. The tests commonly done arranged by order is AFP, CEA, β-hCG, tPSA. The rarely test is CA125, CA19-9, CA15-3, especially in fPSA as shown in Table 2-9 . The major common instrument are Abbott AxSYM and Elecsys in all markers as shown in Figure 2. Seven out of 70 laboratories are participate international EQA in tumor marker scheme. Fifty four out of 70 laboratories need to join in our EQA in tumor marker scheme as shown in Table 10 . As a result of there are very less laboratories perform fPSA, so our EQA in tumor marker scheme consisting of AFP, CEA, PSA, CA125, CA15-3, CA19-9 and β-hCG is established.

Table 1. Number of sent and returned questionnaires classified by hospital size, type and geographic location.

Hospital	**Questionnaire**		
Classified by size	**Number of Sent**	**Number of Returned**	**Returned (%)**
Community hospital (<120 beds)	154	40	26.0%
General hospital (120-500 beds)	149	62	41.6%
Regional hospital (>500 beds)	36	14	38.9%
Other (0 bed)	61	13	21.3%
Total	400	129	32.2%
Classified by type	**Number of Sent**	**Number of Returned**	**Returned (%)**
Government hospital	225	63	28.0%
Private hospital	175	66	37.7%
Total	400	129	32.2%
Classified by geographic location	**Number of Sent**	**Number of Returned**	**Returned (%)**
Bangkok	112	35	31.2%
Outside Bangkok metropolitan	288	94	32.6%
Total	400	129	32.2%

Table 2. Number of laboratories performed AFP assay classified by hospital size, type and geographic location.

		Other		< 120 beds		120–500 beds		> 500 beds	
		No.	%	No.	%	No.	%	No.	%
Bangkok	Government	0	0	0	0	0	0	2	3.1
	Private	5	7.8	4	6.2	12	18.7	2	3.1
Other provinces	Government	1	1.6	1	1.6	17	26.6	7	10.9
	Private	2	3.1	2	3.1	9	14.1	0	0

Total number of laboratory performed AFP is 64.

Table 3. Number of laboratories performed CEA assay classified by hospital size, type and geographic location.

		Other		< 120 beds		120–500 beds		> 500 beds	
		No.	%	No.	%	No.	%	No.	%
Bangkok	Government	1	1.6	0	0	0	0	2	3.2
	Private	5	8.1	3	4.8	12	19.4	2	3.2
Other provinces	Government	1	1.6	1	1.6	16	25.8	7	11.3
	Private	2	3.2	2	3.2	8	12.9	0	0

Total number of laboratory performed CEA is 62.

Table 4. Number of laboratories performed tPSA assay classified by hospital size, type and geographic location.

		Other		< 120 beds		120–500 beds		> 500 beds	
		No.	%	No.	%	No.	%	No.	%
Bangkok	Government	1	2.2	0	0	0	0	2	4.4
	Private	5	11.1	1	2.2	13	28.9	1	2.2
Other provinces	Government	1	2.2	1	2.2	4	8.9	7	15.6
	Private	2	4.4	1	2.2	6	13.3	0	0

Total number of laboratory performed tPSA is 45.

Table 5. Number of laboratories performed fPSA assay classified by hospital size, type and geographic location.

		Other		< 120 beds		120–500 beds		> 500 beds	
		No.	%	No.	%	No.	%	No.	%
Bangkok	Government	0	0	0	0	0	0	1	5.6
	Private	0	0	0	0	1	5.6	1	5.6
Other provinces	Government	0	0	0	0	1	5.6	1	5.6
	Private	2	11.1	2	11.1	9	50.0	0	0

Total number of laboratory performed fPSA is 18.

Table 6. Number of laboratories performed CA125 assay classified by hospital size, type and geographic location.

		Other		< 120 beds		120–500 beds		> 500 beds	
		No.	%	No.	%	No.	%	No.	%
Bangkok	Government	0	0	0	0	0	0	2	10.0
	Private	3	15.0	1	5.0	4	20.0	1	5.0
Others provinces	Government	1	5.0	0	0	3	15.0	3	15.0
	Private	1	5.0	1	5.0	0	0	0	0

Total number of laboratory performed CA125 is 20.

Table 7. Number of laboratories performed CA15-3 assay classified by hospital size, type and geographic location.

		Other		< 120 beds		120–500 beds		> 500 beds	
		No.	%	No.	%	No.	%	No.	%
Bangkok	Government	0	0	1	6.7	0	0	1	6.7
	Private	3	20.0	1	6.7	4	26.7	1	6.7
Others provinces	Government	1	6.7	0	0	1	6.7	2	13.3
	Private	1	6.7	0	0	0	0	0	0

Total number of laboratory performed CA15-3 is 15.

Table 8. Number of laboratories performed CA19-9 assay classified by hospital size, type and geographic location.

		Other		< 120 beds		120–500 beds		> 500 beds	
		No.	%	No.	%	No.	%	No.	%
Bangkok	Government	0	0	0	0	0	0	2	11.8
	Private	3	17.6	1	5.9	4	23.5	1	5.9
Other provinces	Government	0	0	0	0	2	11.8	3	17.6
	Private	1	5.9	0	0	0	0	0	0

Total number of laboratory performed CA19-9 is 17.

Table 9. Number of laboratories performed β-hCG assay classified by hospital size, type and geographic location.

		Other		< 120 beds		120–500 beds		> 500 beds	
		No.	%	No.	%	No.	%	No.	%
Bangkok	Government	0	0	0	0	0	0	1	2.2
	Private	4	8.8	0	0	8	17.8	2	4.4
Other provinces	Government	1	2.2	1	2.2	17	37.8	6	13.3
	Private	2	4.4	1	2.2	2	4.4	0	0

Total number of laboratory performed β-hCG is 45.

Table 10. Numbers and percentages of laboratories who participated to international EQAS and EQAT scheme classified by type, size and geographic location

	International EQA membership*		**Interested to join our scheme***	
	Number	**%**	**Number**	**%**
Government	4	6.0%	27	40.3%
Private	3	4.5%	27	40.3%
No bed	0	0%	7	10.4%
<120 beds	2	3%	5	7.5%
120-500 beds	1	1.5%	31	46.3%
>500 beds	4	6.0%	11	16.4%
Bangkok	5	6.0%	19**	27.9%
Outside Bangkok metropolitan	2	3.0%	35**	51.5%

* Answer from 67 laboratories

** Answer from 68 laboratories

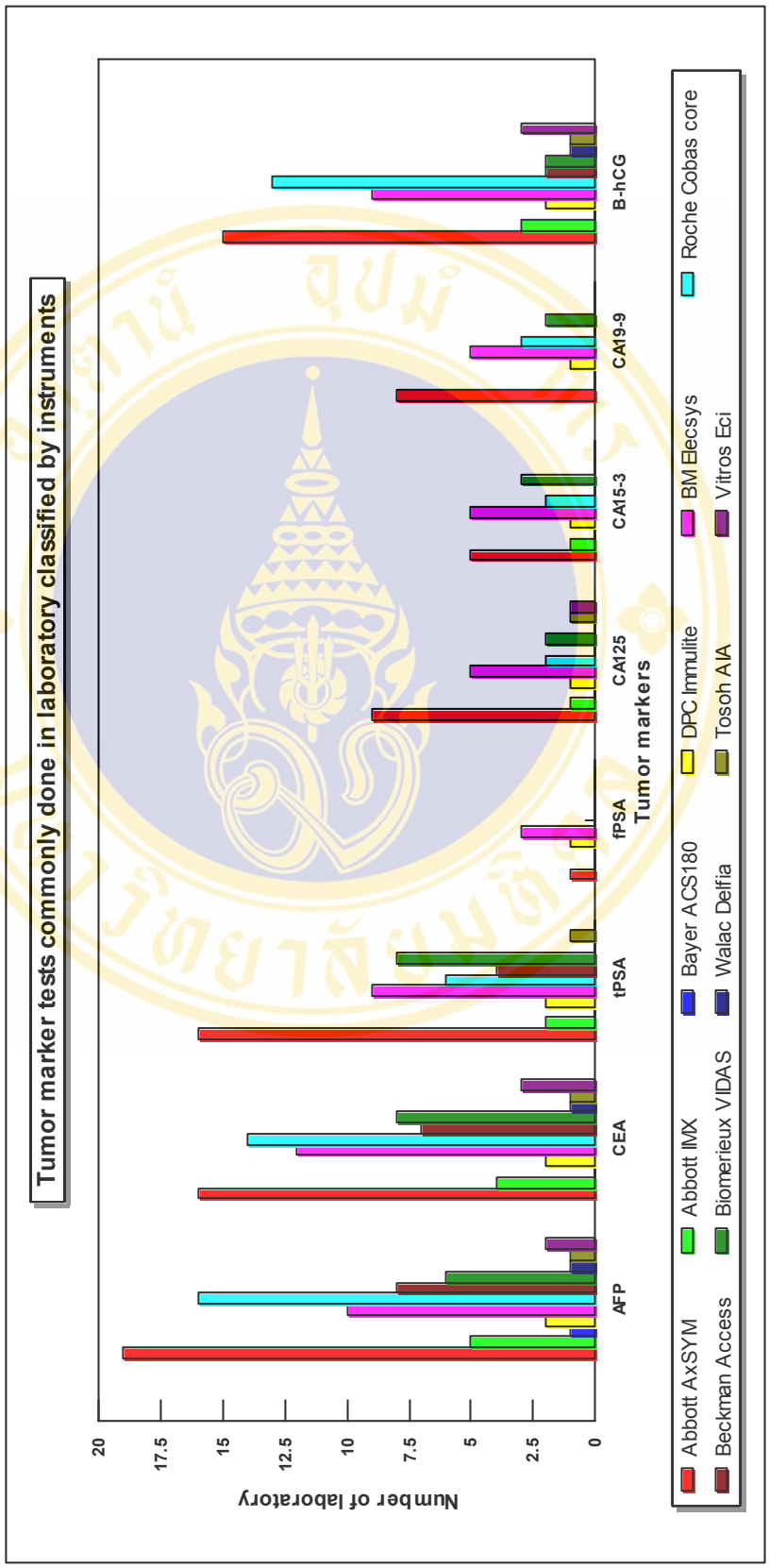

Figure 2. Tumor marker tests commonly done in laboratories classified by instruments

2. Control material selection

Two levels of lyophilized and 0.2% preserved Bronidox liquid form were examined. After storage on 0, 1 , 5, 7, 8, 10, 12, 13, 15, 20, 30, 45, 60 day, at 4°C and room temperature (25°C - 30°C) and in condition of before and after round-trip mailing, the stability of control sera were evaluated against RCV. The result of the sample stored at 4°C and room temperature and in condition of before and after round-trip mailing show in Table 24-34 in Appendix. If there is the deviation of a result more than RCV at day interval, the control sera are judge as instability. The result show that liquid form keep at 4 ° C and room temperature and be used until day 1 as shown in Figure 3-4, but lyophilized form can be used up to 60 day as shown in Figure 5-6 . So the lyophilized control sera should be selected in our EQA in tumor marker scheme.

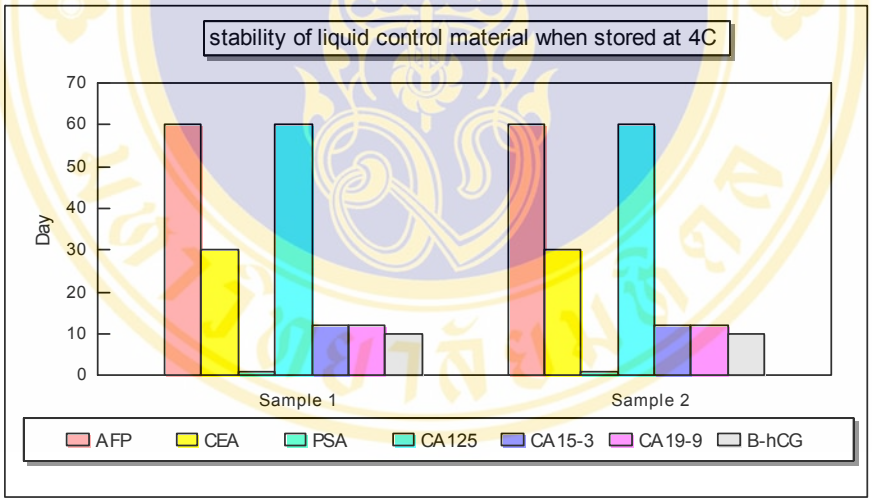

Figure 3. Stability of control sera in liquid form when stored at 4°C

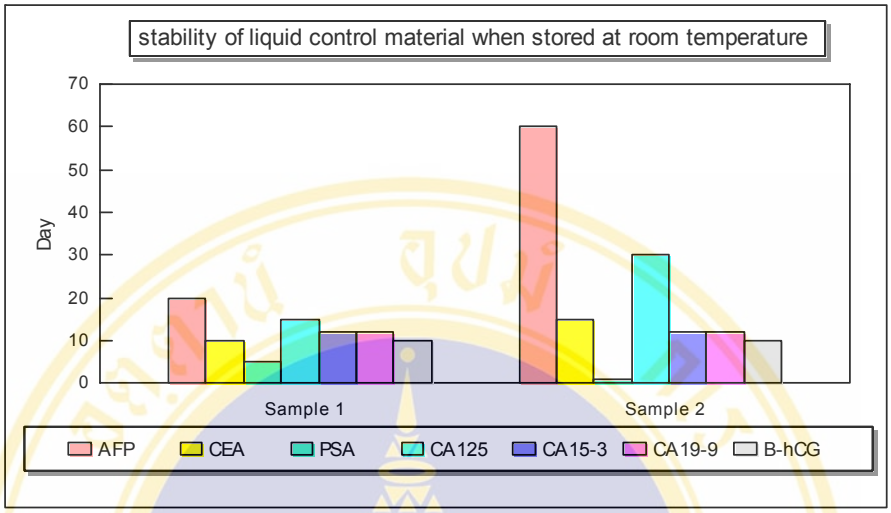

Figure 4. Stability of control sera in liquid form when stored at room temperature

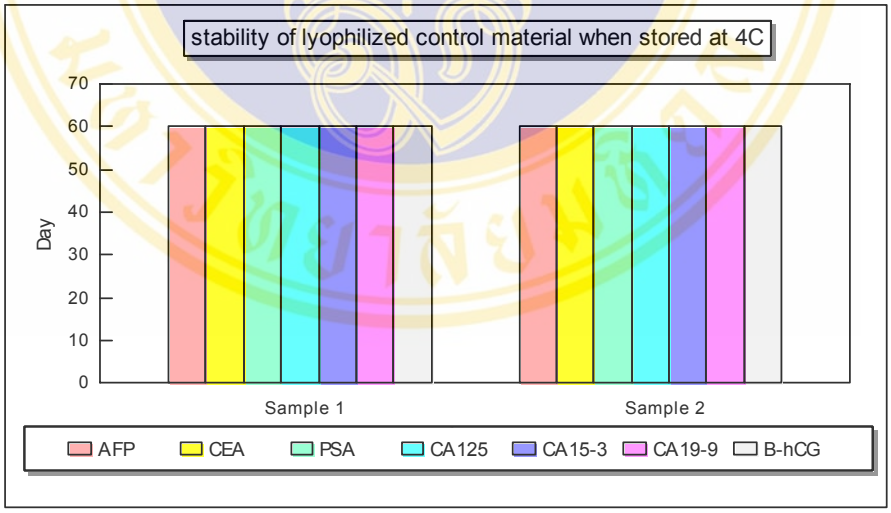

Figure 5. Stability of control sera in lyophilized form when stored at 4° C

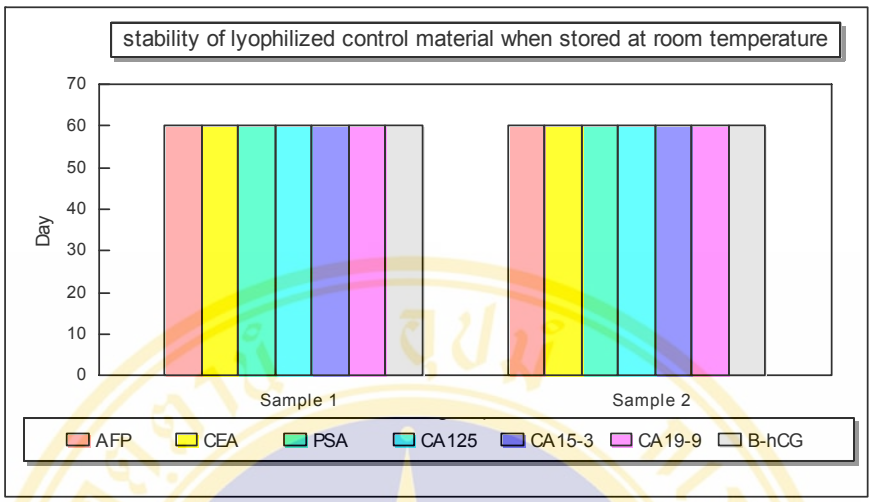

Figure 6. Stability of control sera in lyophilized form when stored at room temperature

3. EQAT pilot project

Requested form and assessment report form as shown in Figure 22, 23A-23H as shown in Appendix were attached together with lyophilized control serum in every trials, with exception of first trial omitted assessment report form. This pilot project consists of 6 trials; 12 samples. Each sample consists of 1.0 ml. The dispatched date and result-reported form received date at organization of the 6 trials are indicated in Table 11. The analyzed result of an individual participant reported on requested form was sent out to organizer as soon as possible. Then, participant returned results were analysis and sent to the participants soon after the analysis of the participant returned results were accomplished.

Seventy two laboratories joined EQAT pilot project. Among these, 32 laboratories (44.4%) located in Bangkok, 40 laboratories (55.6%) located in every regions of Thailand. Among these, 35 laboratories (48.6%) available in private hospitals, 37 laboratories (51.1%) is a government hospitals. According to the size 11 laboratories (15.3%) is a private laboratory, 8 laboratories (11.1%) have less than 120 beds, 36 laboratories (50%) have 120-500 beds, and 17 laboratories (23.6%) have more than 500 beds as summarized in Table 12. There were 63 – 64 out of 72 laboratories return results (response rate = 88.9%) as shown in Table 13.

The total number of tumor marker testing in each trial were summarized in Table 13. It is indicated that AFP and CEA is the major common tumor markers, the minor common group is PSA and β-hCG, the rarely is the group of CA antigen.

Table 11. Dispatched date and dateline date for returning result-report form

Trial ID	Sample dispatched date	Dateline date
Trial 1	16 Dec 2002	5 Jan 2003
Trial 2	6 May 2003	6 Jun 2003
Trial 3	8 Jul 2003	21 Jul 2003
Trial 4	11 Sep 2003	25 Sep 2003
Trial 5	13 Oct 2003	3 Nov 2003
Trial 6	11 Dec 2003	31 Dec 2003

Table 12. Members of EQAT pilot project classified by hospital size, type, and geographic location.

Hospital	Number	(%)
Classified by size		
Community hospital (<120 beds)	8	11.1%
General hospital (120-500 beds)	36	50.0%
Regional hospital (>500 beds)	17	23.6%
Other (0 bed)	11	15.3%
Total	72	100%
Classified by type		
Government hospital	37	51.4%
Private hospital	35	48.6%
Total	72	100%
Classified by geographic location		
Bangkok	32	44.4%
Outside Bangkok metropolitan	40	55.6%
Total	72	100%

Table 13. Tumor markers performed by members of EQAT pilot project in each trial.

Trial	AFP	CEA	PSA	CA125	CA15-3	CA19-9	β-hCG	Returned result*
Trial 1	55	52	41	19	13	17	38	63
Trial 2	52	51	39	17	13	16	43	64
Trial 3	51	50	40	16	11	14	45	64
Trial 4	52	50	42	15	11	11	45	64
Trial 5	57	54	47	21	15	15	48	64
Trial 6	55	53	44	20	13	15	45	62

* Number of EQAT members is 72.

3.1 EQAT pilot project : first trial

In trial 1, two specimens identified as sample 1 and 2 were sent to participant on 16 Dec 2002. The deadline date is 5 Jan 2003 as shown in Table 11. All 2 specimens would come into account for tumor marker test that laboratory serve in routine work. There were 63 (87.5%) out of 72 laboratories returned the result in this trial. The used instrument in this trial was shown Figure 7. The tumor marker tests that laboratories commonly done arranged from popular one is AFP, CEA, PSA, β-hCG, CA125, CA19-9, and rarely CA15-3 as shown in Table 13.

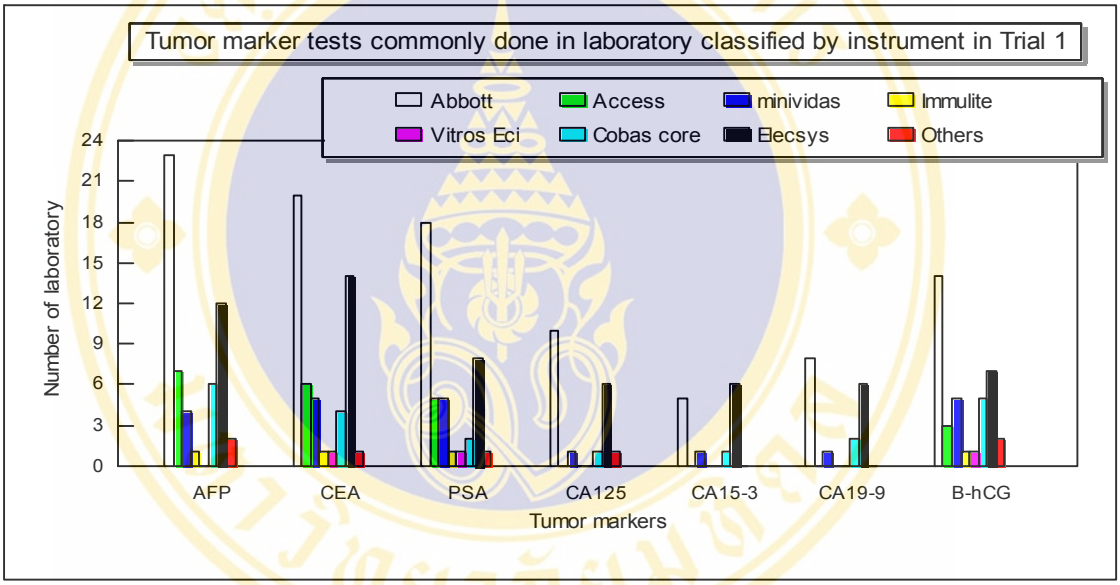

Figure 7. Tumor marker testing classified by instruments in trial 1

The %CV of all tumor markers were shown in Table 14 – 17, Figure 8. In sample 1, Abbott AxSYM has highest %CV (participants n< 3 exclusion) for CEA (13.1%), PSA (13.8%), CA125 (18.1%), and CA19-9 (22.5%). Cobas core has highest %CV in AFP (16.0%), and β-hCG (10.8%). Elecsys has highest %CV in CA15-3 (7.3%). In sample 2, Abbott AxSYM has highest %CV for PSA (24.7%), CA125 (14.3%), CA15-3 (9.9%), CA19-9 (13.2%). Cobas core has highest %CV for AFP (13.6%), and CEA (14.4%). Beckman Access has highest %CV for β-hCG (23.0%). On the other hand, in sample 1, Elecsys has lowest %CV for AFP (8.2%), CA125 (0.0%), CA19-9 (8.6%). Minividas has lowest %CV for CEA (4.2%), β-hCG (2.1%). Beckman Access has lowest %CV for PSA (4.2%). In sample 2, Elecsys has lowest %CV for CA125

(6.4%), CA15-3 (6.9%), CA19-9 (4.1%), and β-hCG (2.3%). Minividas has lowest %CV for CEA (3.4%), and PSA (0.0%). Beckman Access has lowest %CV for AFP (4.4%).

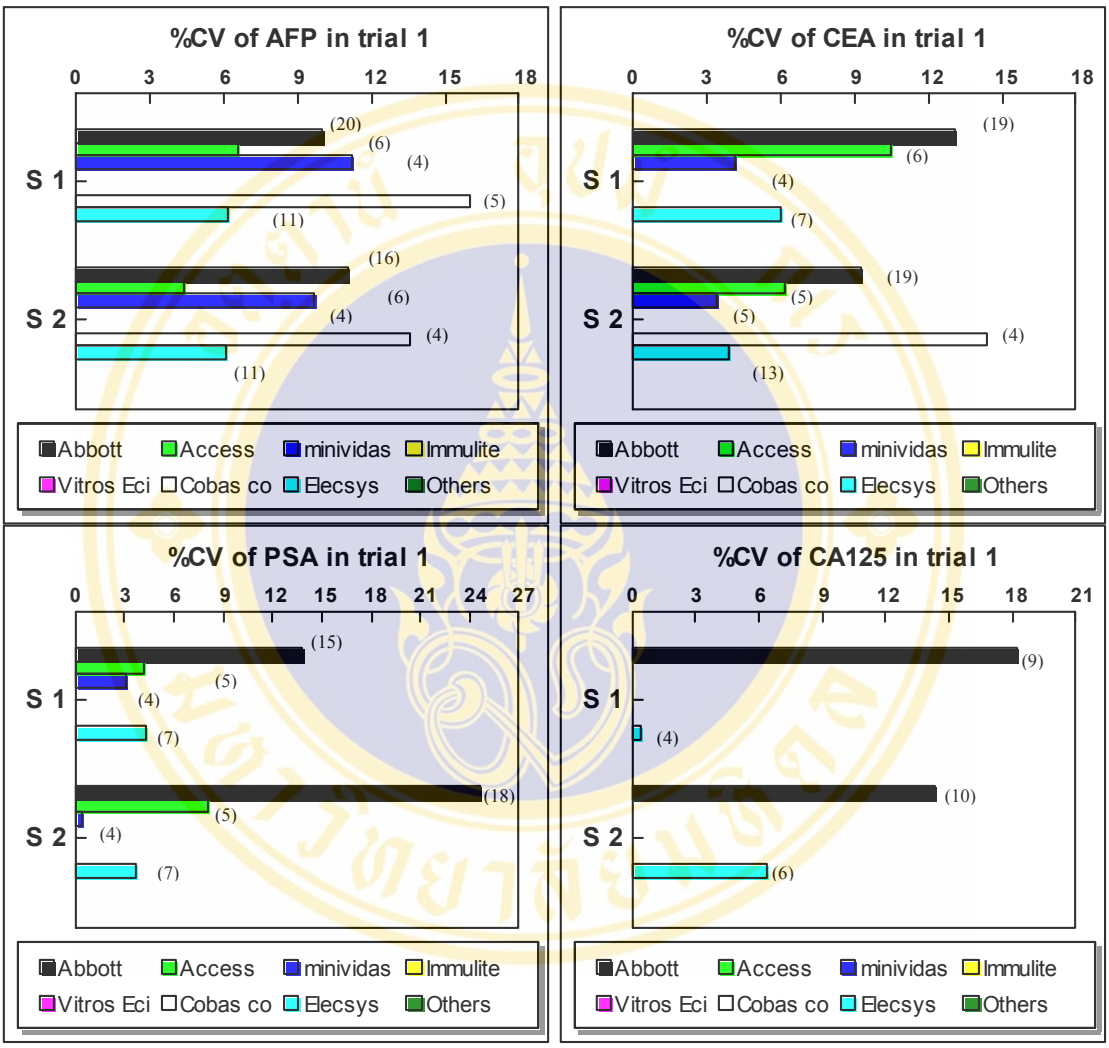

Figure 8. %CV of each instrument in trial 1

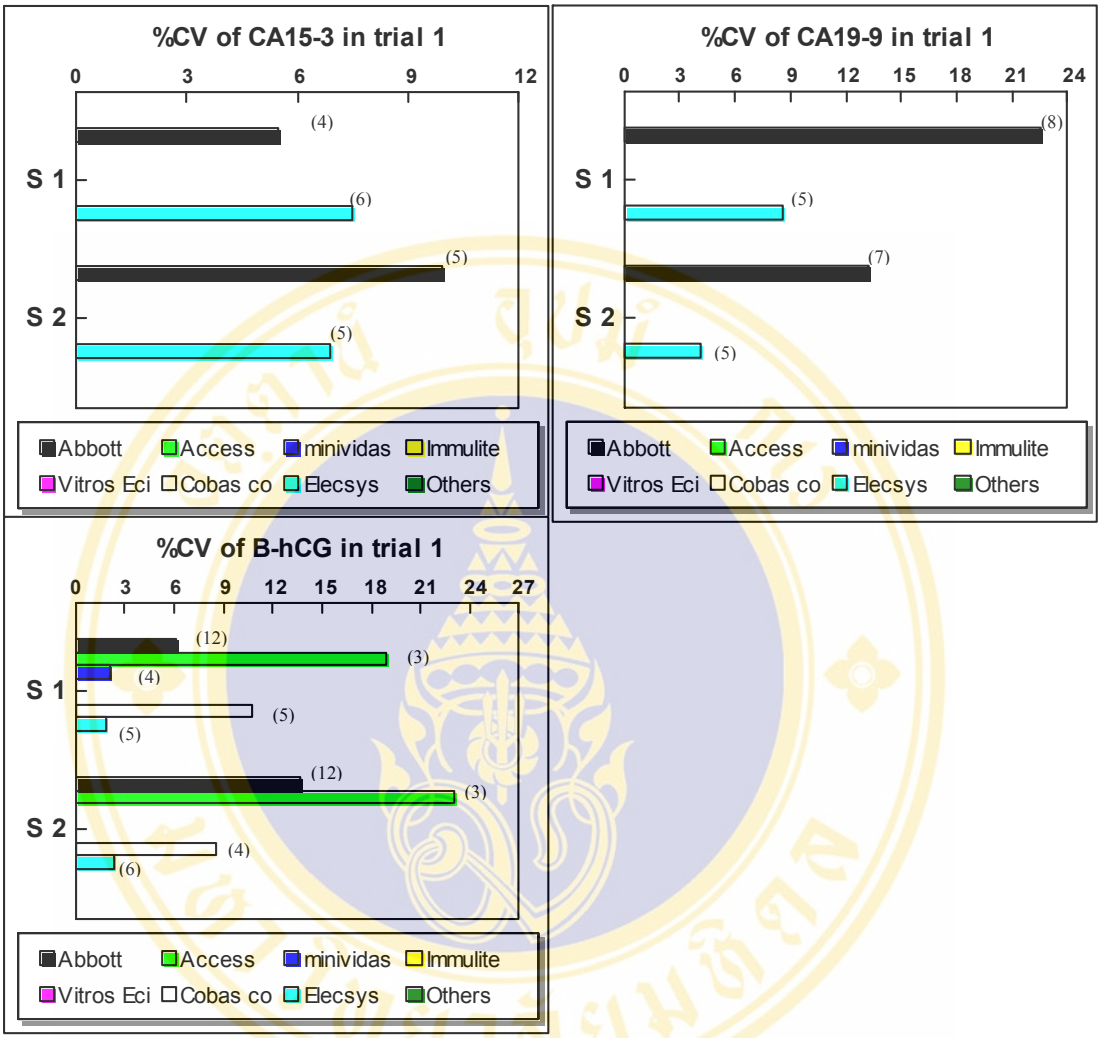

Figure 8. %CV of each instrument in trial 1 (Cont.)

3.2 EQAT pilot project : Second trial

For trial 2, this was done in 6 May 2003 and ask for submitted result on 6 June 2003 as shown in Table 11. Sixty four (88.9%) of participant submitted their results. The tumor marker tests that commonly do and the number of automate analyzer pattern still the same in trial 1 as shown in Figure 9.

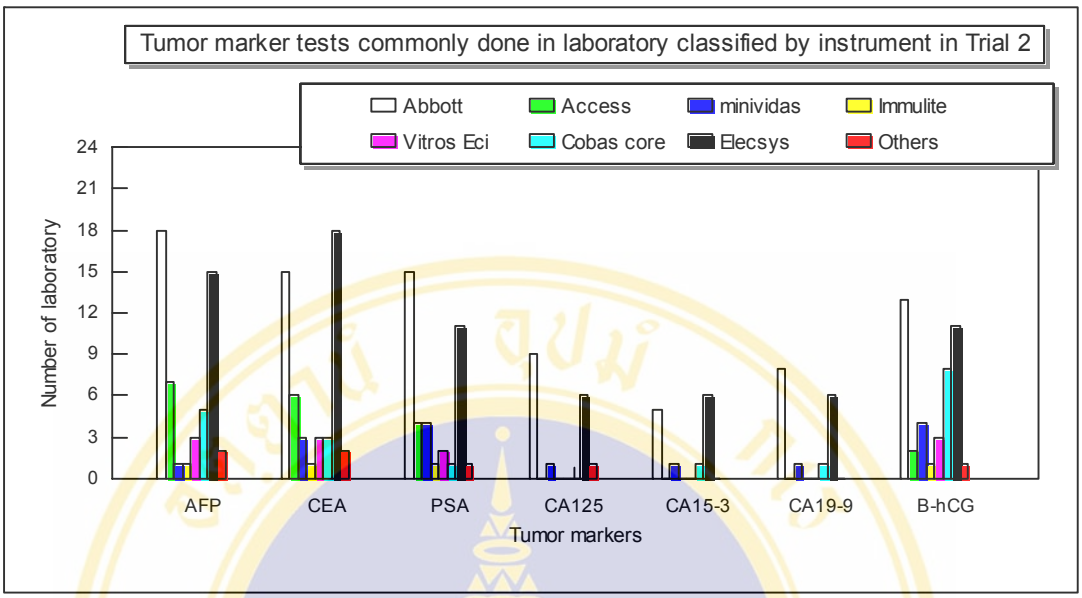

Figure 9. Tumor marker testing classified by instruments in trial 2.

The %CV of all tumor markers were shown in Table 14 – 17, Figure 10. In sample 3, Abbott AxSYM has highest %CV for PSA (18.2%), CA125 (13.3%), CA15-3 (11.9%), and CA19-9 (7.5%). Minividas has highest %CV for CEA (16.4%), and β-hCG (8.1%). Cobas core has highest %CV for AFP (21.6%). In sample 4, Abbott AxSYM has highest %CV for PSA (14.1%), CA125 (11.2%), CA15-3 (11.8%), CA19-9 (5.2%), and β-hCG (9.7%). Cobas core has highest %CV for AFP (13.2%). Minividas has highest %CV for CEA (15.7%). In contrast, in sample 3, Elecsys has lowest %CV for AFP (7.0%), CA125 (6.1%), CA15-3 (6.8%), and CA19-9 (5.2%). Vitros Eci has lowest %CV for CEA (2.3%). Beckman Access has lowest %CV for PSA (4.9%). Cobas core has lowest %CV for β-hCG (4.7%). In sample 4, Elecsys has lowest %CV for AFP (6.7%), CA125 (4.4%), CA15-3 (8.3%), and CA19-9 (4.0%). Cobas core has lowest %CV for CEA (6.8%), and β-hCG (5.0%). Beckman Access has lowest %CV for PSA (5.3%).

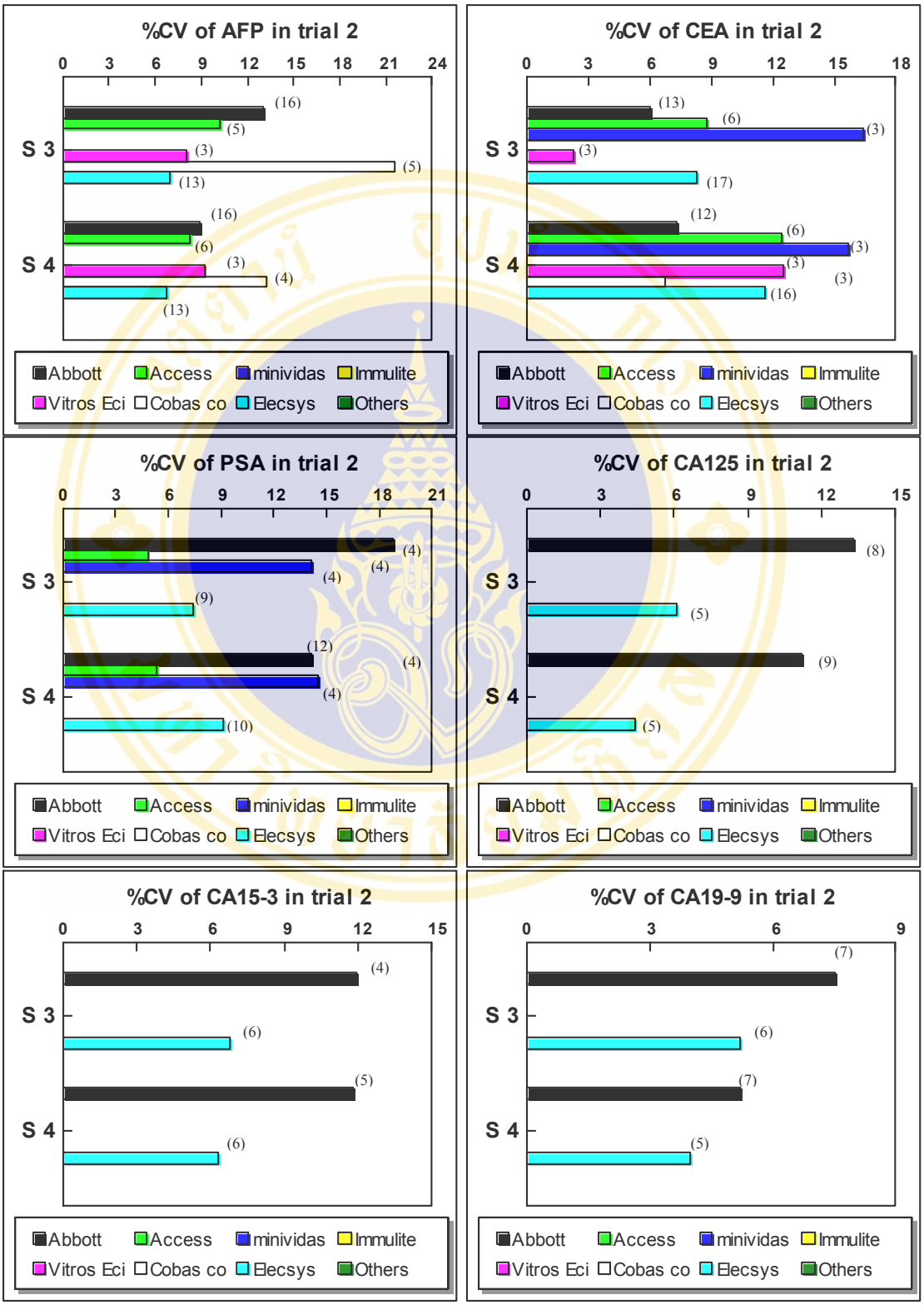

Figure 10. %CV of each instrument in trial

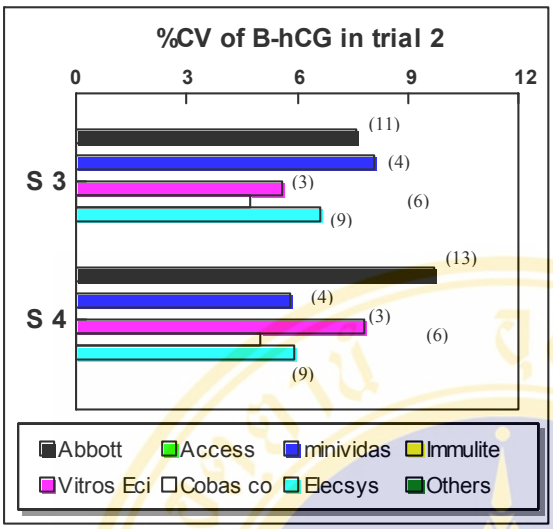

Figure 10. %CV of each instrument in trial 2 (Cont.)

3.3 EQAT pilot project : Third trial

For trial 3, this was done in 8 Jun 2003 and also ask for return result on 21 Jul 2003 as shown in Table 11. Sixty four (88.9%) of laboratories submitted their result. The use of automate analyzer is differ from those of previous trial. The Elecsys is the most popular automate analyzer. The second is Abbott AxSYM as shown in Figure 11. The tumor marker tests that commonly do still the same.

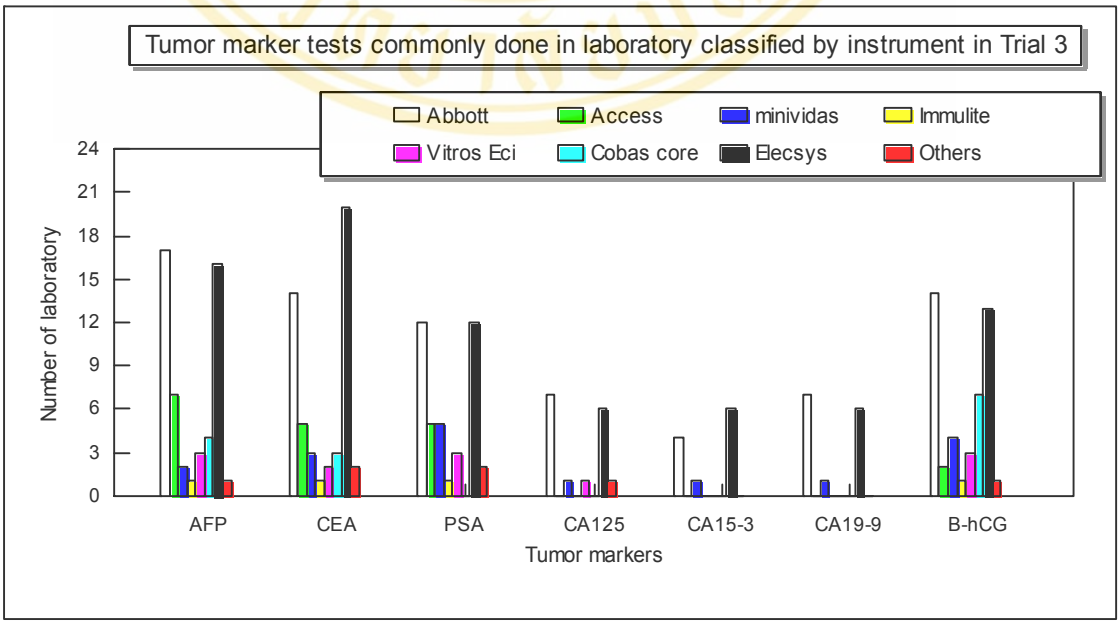

Figure 11. Tumor marker testing classified by instruments in trial 3

The %CV of all tumor markers were shown in Table 14 – 17, Figure 12. In sample 5, Abbott AxSYM has highest %CV for PSA (10.6%), CA125 (8.8%), CA19-9 (11.6%), and β-hCG (8.5%). Cobas core has highest %CV for AFP (14.6%), and CEA (8.1%). Elecsys has highest %CV for CA15-3 (5.5%). In sample 6, Abbott AxSYM has highest %CV for PSA (17.9%), CA125 (8.2%), and CA19-9 (13.9%). Cobas core has highest %CV for AFP (16.7%), and β-hCG (9.9%). Elecsys has highest %CV for CEA (10.6%), and CA15-3 (7.1%). On the other hand, in sample 5, Elecsys has lowest %CV for AFP (5.6%), CA125 (3.0%), CA19-9 (4.2%) and β-hCG (3.8%). Beckman Access has lowest %CV for CEA (5.9%). Minividas has lowest %CV for PSA (2.9%). Abbott AxSYM has lowest %CV for CA15-3 (4.1%). In sample 6, Elecsys has lowest %CV for AFP (6.9%), CA125 (3.1%), CA19-9 (3.9%) and β-hCG (5.2%). Cobas core has lowest %CV for CEA (2.2%). Minividas has lowest %CV for PSA (5.1%). Abbott AxSYM has lowest %CV for CA15-3 (3.1%).

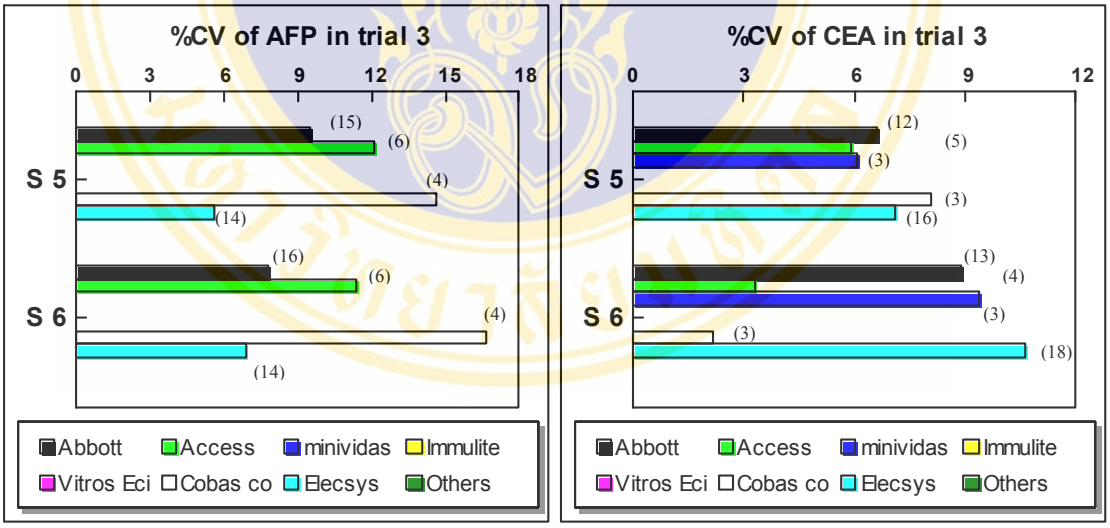

Figure 12. %CV of each instrument in trial

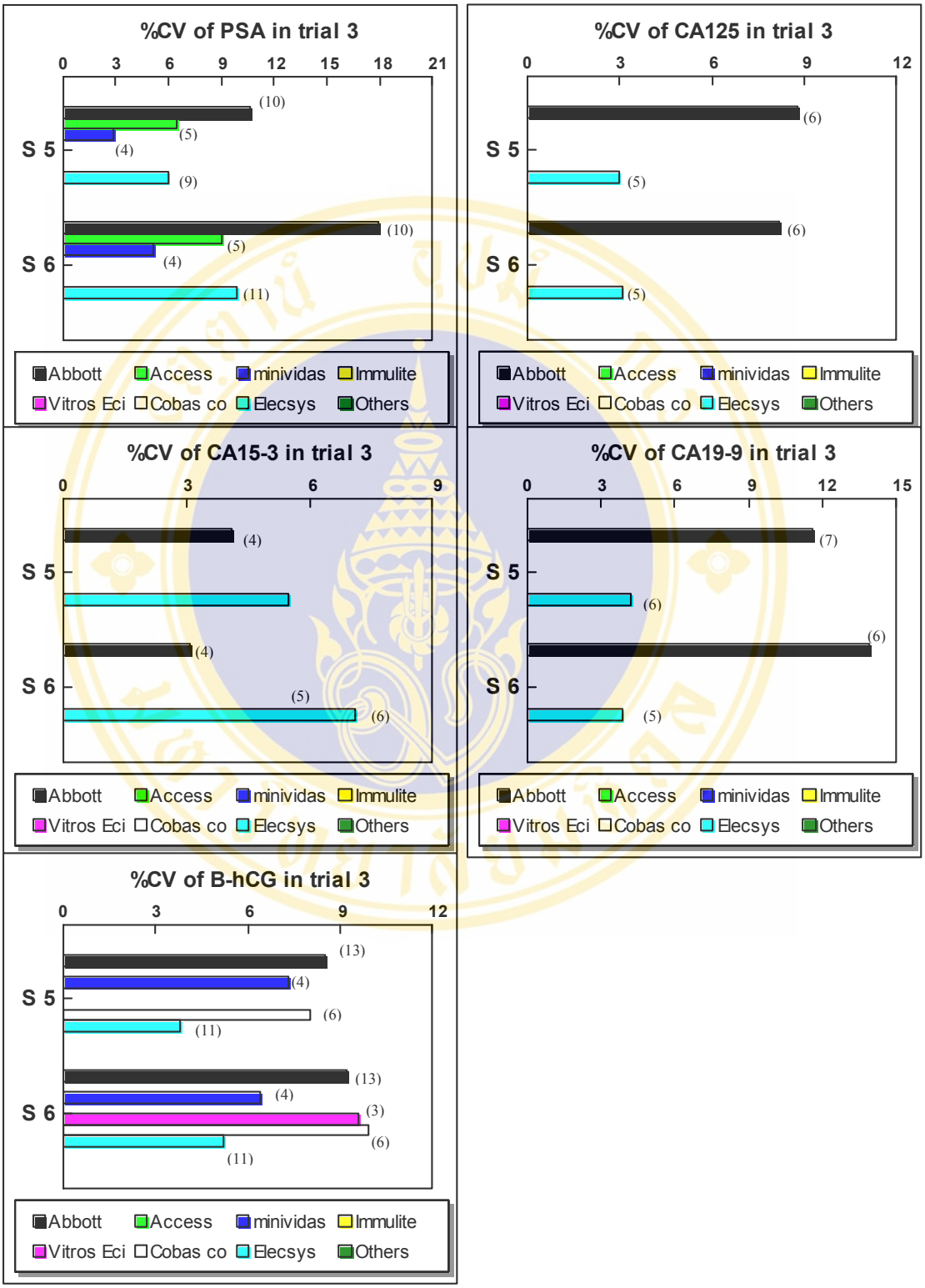

Figure 12. %CV of each instrument in trial 3 (Cont.)

3.4 EQAT pilot project : Fourth trial

For trial 4, this was done in 11 September 2003 and ask for return result on 25 September 2003 as shown in Table 11. Sixty four (88.9%) out of laboratories submitted their result. the use of automate analyzer and the tumor marker that commonly do are the same as trial 1 and 2 as shown in Figure 13.

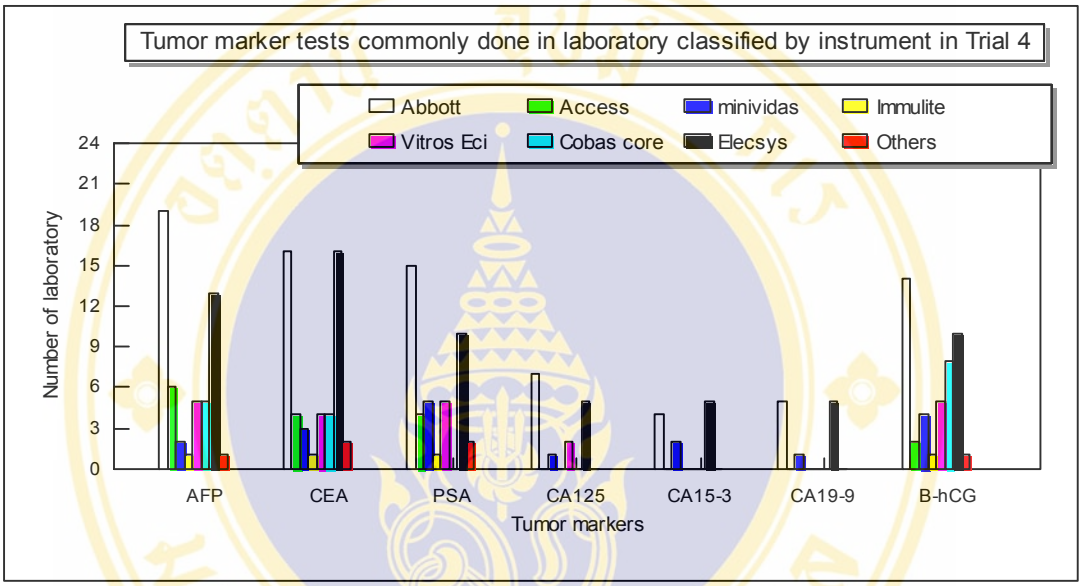

Figure 13. Tumor marker testing classified by instrument in trial 4

The %CV of all tumor markers were shown in Table 14 – 17, Figure 14. In sample 7, Cobas core has highest %CV for AFP (17.2%), CEA (30.2%), and β-hCG (24.2%). Abbott AxSYM has highest %CV for PSA (19.6%), CA125 (8.5%), and CA19-9 (9.8%). Elecsys has highest %CV for CA15-3 (8.6%). In sample 8, Cobas core also has highest %CV for AFP (34.2%), CEA (31.4%), and β-hCG (24.4%). Elecsys has highest %CV for CA125 (5.5%), CA15-3 (11.1%), and CA19-9 (5.3%). In contrast, in sample 7, Elecsys has lowest %CV for CA125 (7.3%), CA19-9 (2.8%), and β-hCG (5.3%). Beckman Access has lowest %CV for AFP (5.5%), and PSA (4.8%). Abbott AxSYM has lowest %CV for CEA (5.5%) ,and CA15-3 (8.2%). In sample 8, Abbott AxSYM has lowest %CV for CA125 (2.5%), CA15-3 (9.2%), and CA19-9 (3.8%). Elecsys has lowest %CV for PSA (4.3%), and β-hCG (4.9%). Vitros Eci has lowest %CV for AFP (9.5%). Minividas has lowest %CV for CEA (4.4%).

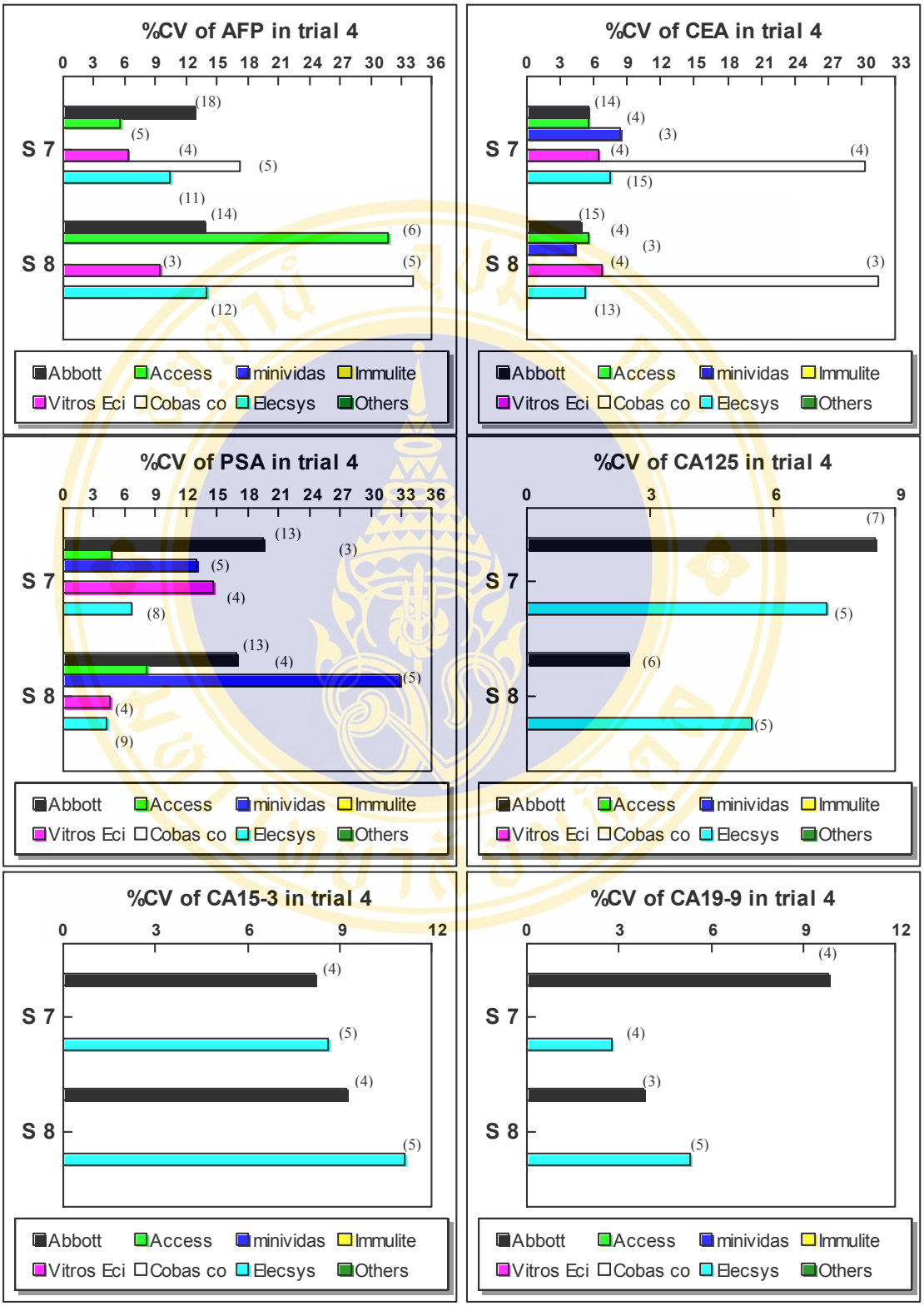

Figure 14. %CV of each instrument in trial

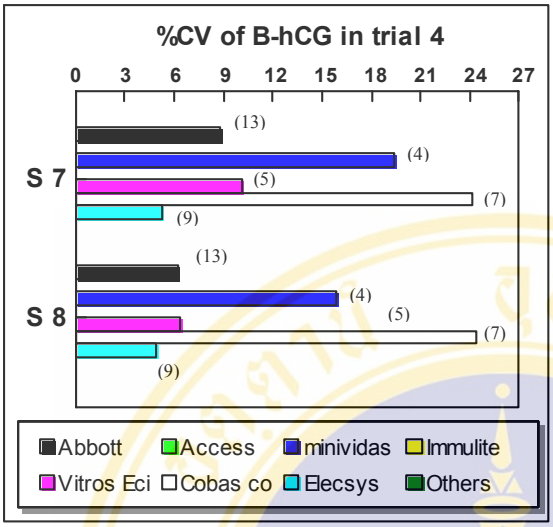

Figure 14. %CV of each instrument in trial 4 (Cont.)

3.5 EQAT pilot project : Fifth trial

For trial 5, the control sera were dispatched in 13 Oct 2003. The deadline date is 3 Nov 2003 as shown in Table 11. Sixty four (88.9%) submitted their result. AFP is the tumor marker commonly done. Abbott AxSYM is the most popular method and the second one is BM Elecsys as shown in Figure 15.

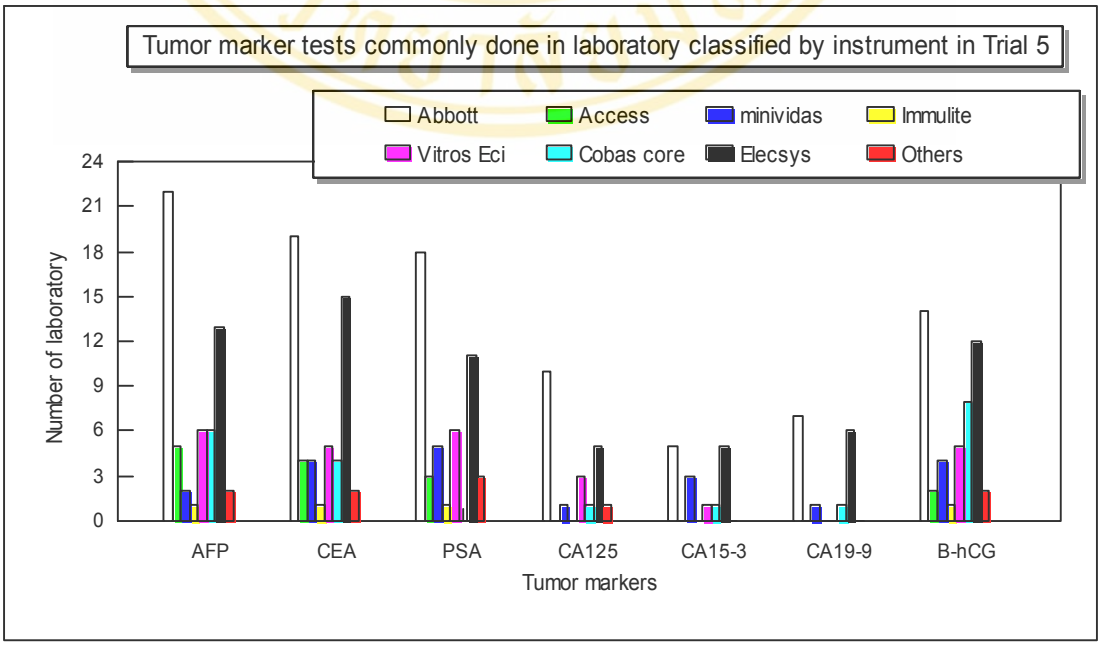

Figure 15. Tumor marker testing classified by instrument in trial

The %CV of all tumor markers were shown in Table 14 – 17, Figure 16. In sample 9, Cobas core has highest %CV for AFP (21.8%), CEA (13.0%), and β-hCG (10.2%). Abbott AxSYM has highest %CV for CA125 (15.4%), and CA15-3 (9.3%). Minividas has highest %CV for PSA (18.9%). Elecsys has highest %CV for CA19-9 (6.6%). In sample 10, Abbott AxSYM has highest %CV for CEA (9.8%), PSA (10.1%), and CA125 (14.7%). Cobas core has highest %CV for AFP (25.9%), and β-hCG (8.1%). Elecsys has highest %CV for CA15-3 (7.8%), and CA19-9 (8.9%). On the other hand, in sample 9, Vitros Eci has lowest %CV for AFP (1.3%), and β-hCG (0.8%). Beckman Access has lowest %CV for CEA (3.5%), and PSA (3.2%). Abbott AxSYM has lowest %CV for CA19-9 (5.5%). In sample 10, Vitros Eci also has lowest %CV for AFP (1.3%), and β-hCG (0.3%). In addition, Vitros Eci has lowest %CV for CA125 (3.6%). Minividas has lowest %CV for PSA (3.6%), and CA15-3 (4.3%). Abbott AxSYM has lowest %CV for CA19-9 (7.4%).

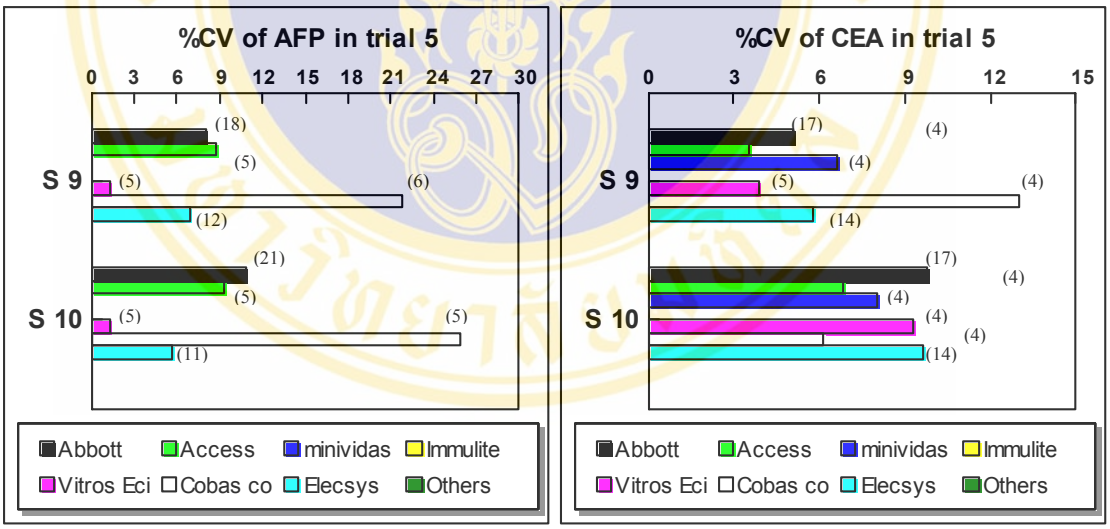

Figure 16. %CV of each instrument in trial 5

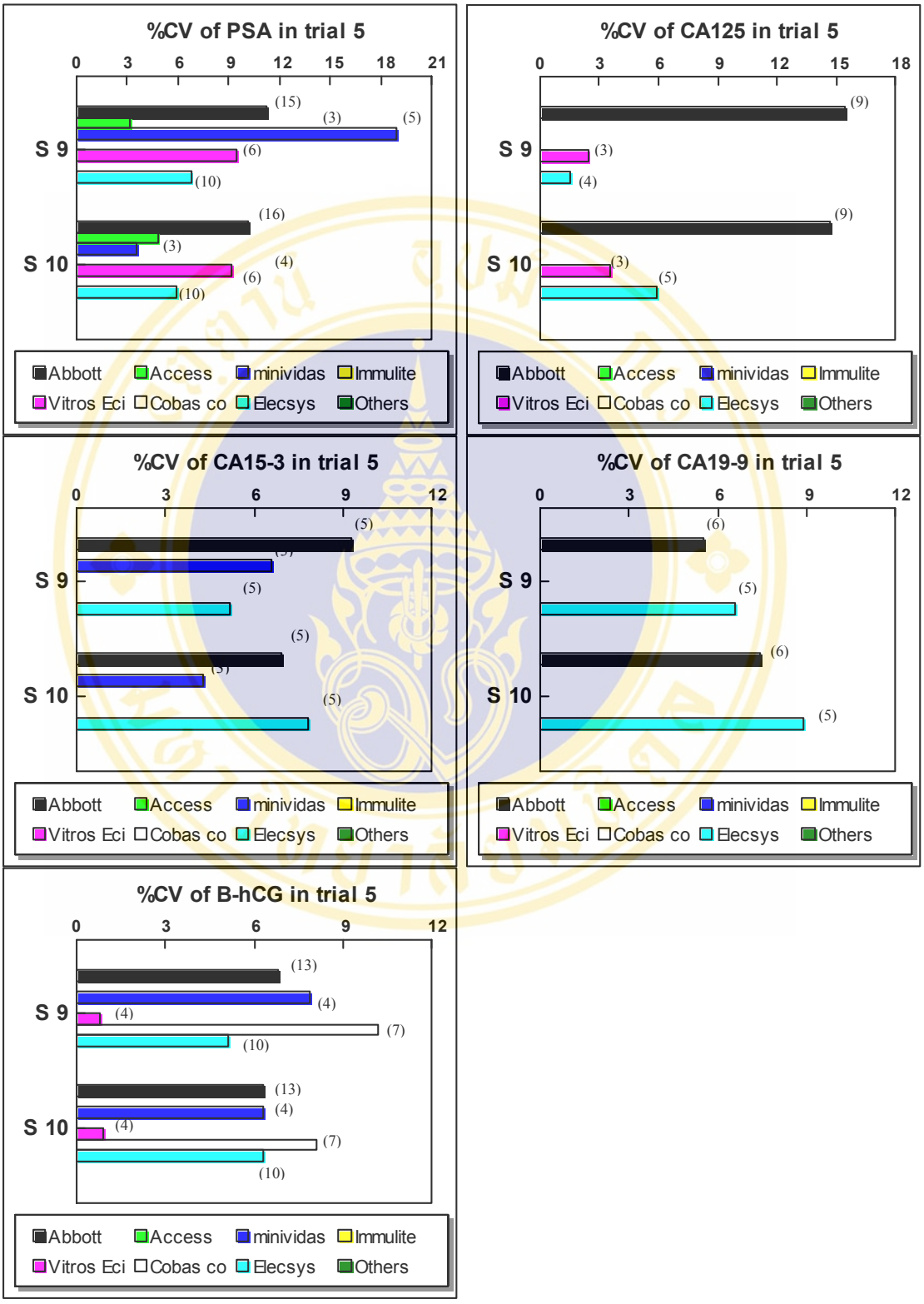

Figure 16. %CV of each instrument in trial 5 (Cont.)

3.6 EQAT pilot project : Sixth trial

For trial 6, the control sera were dispatched in 11 Dec 2003. The result was ask for submitted within 31 Dec 2003 as shown in Table 11. Only 62 (86.1%) laboratories submitted their result; however, the use of automate analyzer and the tumor marker that commonly do are the same previous trial as shown in Figure 17.

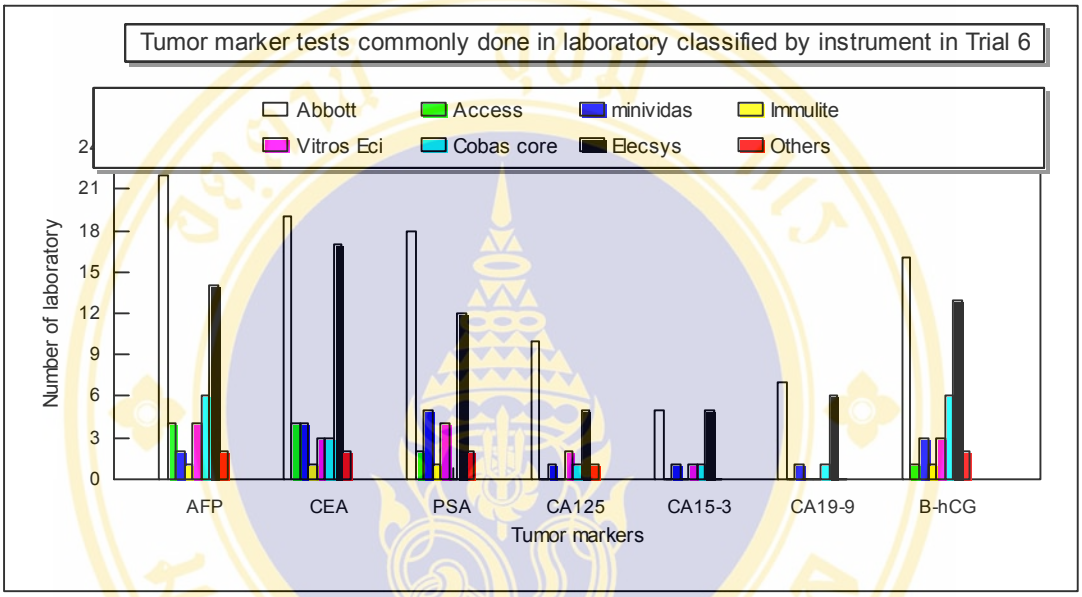

Figure 17. Tumor marker testing classified by instrument in trial 6

The %CV of all tumor markers were shown in Table 14 – 17, Figure 18. In sample 11, Abbott AxSYM has highest %CV for CA125 (9.6%), CA15-3 (13.6%), and CA19-9 (24.4%). Vitros Eci has highest %CV for CEA (32.2%), and PSA (9.2%). Beckman Access has highest %CV for AFP (9.3%). Minividas has highest %CV for β-hCG (12.6%). In sample 12, Abbott AxSYM has highest %CV for CA15-3 (8.8%), and CA19-9 (9.8%). Elecsys has highest %CV for AFP (16.2%), and CA125 (5.1%). Vitros Eci has highest %CV for CEA (24.7%). Minividas has highest %CV for PSA (8.0%). Cobas core has highest %CV for β-hCG (12.3%). On the other hand, in sample 11, Elecsys has lowest %CV for PSA (5.6%), CA125 (3.7%), CA15-3 (4.7%), and CA19-9 (5.5%). Abbott AxSYM has lowest %CV for AFP (8.1%), CEA (6.9%). Vitros Eci has lowest %CV for β-hCG (1.5%). In sample 12, Vitros Eci has lowest %CV for AFP (5.2%), and PSA (1.4%). Elecsys has lowest %CV for CA15-3 (2.8%), and CA19-9 (6.5%). Beckman Access has lowest %CV for CEA (4.5%). Abbott

AxSYM has lowest %CV for CA125 (4.3%).

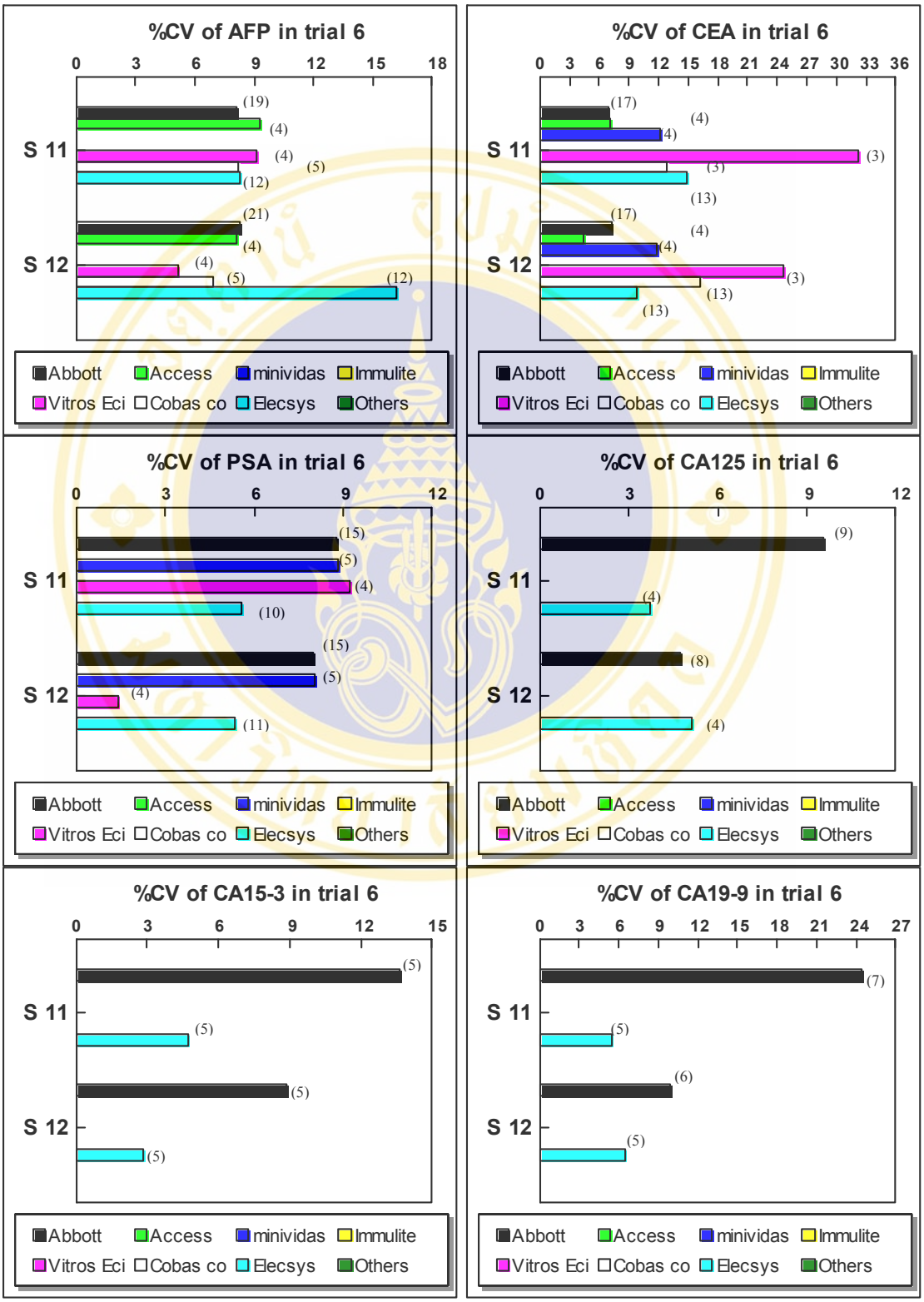

Figure 18. %CV of each instrument in trial 6

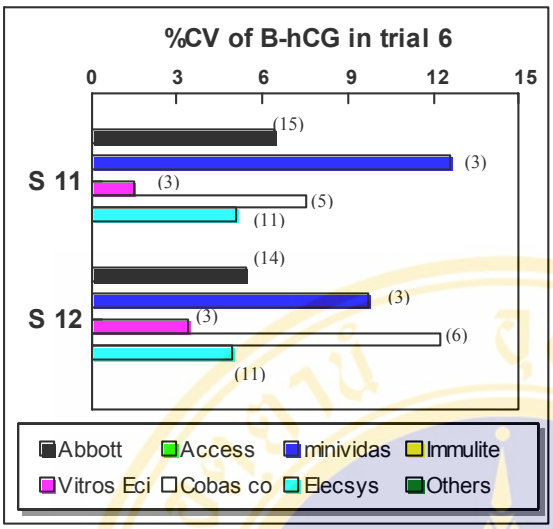

Figure 18. %CV of each instrument in trial 6 (Cont.)

Table 14. % CV of AFP and CEA assays classified by instruments

	Trial 1		Trial 2		Trial 3		Trial 4		Trial 5		Trial 6		Method mean %CV (n)
Sample No.	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**	**S10**	**S11**	**S12**	
AFP	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	
AxSYM / IMX	10.0 (20)	11.1 (16)	13.0 (16)	8.9 (16)	9.5 (15)	7.8 (16)	12.9 (18)	13.8 (14)	8.0 (18)	10.8 (21)	8.1 (19)	8.3 (21)	9.6 (210)
Beckman Access	6.6 (6)	4.4 (6)	10.2 (5)	8.2 (6)	12.1 (6)	11.4 (6)	5.5 (5)	31.7 (6)	8.8 (5)	9.3 (5)	9.3 (4)	8.1 (4)	8.8 (64)
Minividas	11.2 (4)	9.7 (4)											* (8)
Vitros Eci			8.0 (3)	9.2 (3)			6.4 (4)	9.5 (3)	1.3 (5)	1.3 (5)	9.1 (4)	5.2 (4)	5.7 (31)
Cobas core	16.0 (5)	13.6 (4)	21.6 (5)	13.2 (4)	14.6 (4)	16.7 (4)	17.2 (5)	34.2 (5)	21.8 (6)	25.9 (5)	8.2 (5)	6.9 (5)	15.8 (51)
Elecsys	6.2 (11)	6.1 (11)	7.0 (13)	6.7 (13)	5.6 (14)	6.9 (14)	10.5 (11)	14.0 (12)	6.9 (12)	5.6 (11)	8.3 (12)	16.2 (12)	7.6 (146)
Mean	10.0 (46)	9.0 (41)	12.0 (42)	9.2 (42)	10.4 (39)	10.7 (40)	10.5 (43)	20.6 (40)	9.4 (46)	10.6 (47)	8.6 (44)	8.9 (46)	9.5 (516)
	Trial 1		**Trial 2**		**Trial 3**		**Trial 4**		**Trial 5**		**Trial 6**		**Method mean %CV (n)**
Sample No.	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**	**S10**	**S11**	**S12**	
CEA	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	
AxSYM / IMX	13.1 (19)	9.3 (19)	6.0 (13)	7.3 (12)	6.6 (12)	8.9 (13)	5.5 (14)	4.8 (15)	5.1 (17)	5.8 (17)	6.9 (17)	7.4 (17)	7..6 (185)
Beckman Access	10.5 (6)	6.2 (5)	8.8 (6)	12.4 (6)	5.9 (5)	3.3 (4)	5.6 (4)	5.5 (4)	3.5 (4)	6.8 (4)	7.2 (4)	4.5 (4)	6.7 (56)
Minividas	4.2 (4)	3.4 (5)	16.4 (3)	15.7 (3)	6.1 (3)	9.4 (3)	8.4 (3)	4.4 (3)	6.6 (4)	8.0 (4)	12.1 (4)	11.9 (4)	8.9 (79)
Vitros Eci			2.3 (3)	12.5 (3)			6.4 (4)	6.8 (4)	3.9 (5)	9.3 (4)	32.2 (3)	24.7 (3)	* (29)
Cobas core		14.4 (4)		6.8 (3)	8.1 (3)	2.2 (3)	30.2 (4)	31.4 (3)	13.0 (4)	6.1 (4)	12.9 (3)	16.2 (3)	14.1 (34)
Elecsys	6.0 (7)	3.9 (13)	8.3 (17)	11.6 (16)	7.1 (16)	10.6 (18)	7.5 (15)	5.2 (13)	5.8 (14)	9.6 (14)	14.9 (13)	9.7 (13)	8.4 (222)
Mean	8.4 (36)	7.4 (46)	8.4 (42)	11.0 (43)	6.8 (39)	6.9 (41)	10.6 (44)	9.7 (42)	6.3 (48)	8.3 (47)	14.4 (44)	12.4 (44)	8.0 (605)

Participant n ≥ 3

* Not calculated when numbers of reports were lower than 30

Table 15. % CV of PSA and CA125 assays classified by instruments

	Trial 1		Trial 2		Trial 3		Trial 4		Trial 5		Trial 6		Method mean %CV (n)
Sample No.	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**	**S10**	**S11**	**S12**	
PSA	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	
AxSYM / IMX	13.8 (15)	24.7 (18)	18.8 (14)	14.1 (12)	10.6 (10)	17.9 (10)	19.6 (10)	16.9 (13)	11.2 (15)	10.1 (16)	8.8 (15)	8.0 (15)	14.5
Beckman Access	4.2 (5)	8.1 (5)	4.9 (4)	5.3 (4)	6.5 (5)	9.0 (5)	4.8 (5)	8.2 (4)	3.2 (3)	4.8 (3)			5.9 (41)
Minividas	3.1 (4)	0.0 (4)	14.1 (4)	17.5 (4)	2.9 (4)	5.1 (4)	13.1 (4)	32.8 (5)	18.9 (5)	3.6 (4)	8.8 (5	8.0 (5)	10.4 (53)
Vitros Eci							14.7 (4)	4.6 (4)	9.5 (6)	9.2 (6)	9.2(4)	1.4 (4)	* (28)
Cobas core													
Elecsys	4.3 (7)	3.7 (7)	7.4 (9)	9.1 (10)	6.0 (9)	9.9 (11	6.7 (8)	4.3 (9)	6.8 (10)	5.9 (10)	5.6 (10)	5.3 (11)	6.2 (111)
Mean	6.3 (31)	9.1 (34)	11.3 (31)	11.5 (30)	6.5 (28)	10.5 (30)	11.8 (33)	13.4 (35)	9.9 (39)	6.7 (39)	8.1 (34)	5.7 (35)	9.2 (399)
	Trial 1		**Trial 2**		**Trial 3**		**Trial 4**		**Trial 5**		**Trial 6**		**Method mean %CV (n)**
Sample No.	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**	**S10**	**S11**	**S12**	
CA125	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	
AxSYM / IMX	18.2 (9)	14.3 (10)	13.3 (8)	11.2 (9)	8.8 (6)	8.2 (6)	8.5 (7)	2.5 (6)	14.5 (9)	14.7 (9)	9.6 (9)	4.7 (8)	10.8 (96)
Beckman Access													
Minividas													
Vitros Eci									2.5 (3)	3.6 (3)			* (6)
Cobas core													
Elecsys	0.0 (4)	6.4 (6)	6.1 (5)	4.4 (5)	3.0 (5)	3.1 (5)	7.3 (5)	5.5 (5)	1.5 (4)	5.9 (5)	3.7 (4)	5.1 (4)	4.3 (57)
Mean	9.1 (13)	10.4 (16)	9.7 (13)	7.8 (14)	5.9 (11)	5.6 (11)	7.9 (12)	4.0 (11)	6.5 (16)	8.1 (17)	6.6 (13)	4.9 (12)	7.6 (159)

Participant n ≥ 3

* Not calculated when numbers of reports were lower than 30

Table 16. %CV of CA15-3 and CA19-9 assays classified by instruments

	Trial 1		Trial 2		Trial 3		Trial 4		Trial 5		Trial 6		Method mean %CV (n)
Sample No.	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**	**S10**	**S11**	**S12**	
CA15-3	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	
AxSYM / IMX	5.5 (4)	9.9 (5)	11.9 (4)	11.8 (5)	4.1 (4)	3.1 (4)	8.2 (4)	9.2 (4)	9.3 (5)	6.9 (5)	13.6 (5)	8.8 (5)	8.5 (54)
Beckman Access													
Minividas									6.6 (3)	4.3 (3)			*(6)
Vitros Eci													
Cobas core													
Elecsys	7.5 (6)	6.9 (5)	6.8 (6)	6.3 (6)	5.5 (5)	7..1 (6)	8.6 (5)	11.1 (5)	5.2 (5)	7.8 (5)	4.7 (5)	2.8 (5)	6.7 (79)
Mean	6.5 (10)	8.4 (20)	9.4 (10)	9.0 (11)	4.8 (9)	5.1 (10)	8.4 (9)	10.2 (9)	7.0 (13)	6.3 (13)	9.2 (10)	5.8 (10)	7.6 (139)
	Trial 1		**Trial 2**		**Trial 3**		**Trial 4**		**Trial 5**		**Trial 6**		**Method mean %CV (n)**
Sample No.	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**	**S10**	**S11**	**S12**	
CA19-9	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	
AxSYM / IMX	22.5 (8)	13.2 (7)	7.5 (7)	5.2 (7)	11.6 (7)	13.9 (6)	9.8 (4)	3.8 (3)	5.5 (6)	7.4 (6)	24.4 (7)	9.8 (6)	11.2 (74)
Beckman Access													
Minividas													
Vitros Eci													
Cobas core													
Elecsys	8.6 (5)	4.1 (5)	5.2 (6)	4.0 (5)	4.2 (6)	3.9 (5)	2.8 (4)	5.3 (5)	6.6 (5)	8.9 (5)	5.5 (5)	6.5 (5)	5.5 (56)
Mean	15.6 (13)	8.6 (12)	6.4 (13)	4.6 (12)	7.9 (13)	8.9 (11)	6.3 (8)	4.6 (8)	3.6 (11)	8.2 (11)	15.0 (12)	8.2 (11)	8.3 (130)
Participant n ≥ 3	* Not calculated when numbers of reports were lower than 30												

Table 17. β-hCG %CV in trial of participant laboratories classified by instrument

	Trial 1		Trial 2		Trial 3		Trial 4		Trial 5		Rial 6		Method mean %CV (n)
Sample No.	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**	**S10**	**S11**	**S12**	
β-hCG	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	**%CV (n)**	
AxSYM / IMX	6.1 (12)	13.7 (12)	7.6 (11)	9.7 (13)	8.5 (13)	9.2 (13)	8.8 (13)	6.2 (13)	6.8 (13)	8.3 (13)	6.4 (15)	5.5 (14)	7.9 (155)
Beckman Access	18.9 (3)	23.0 (3)											* (6)
Minividas	2.1 (4)		8.1 (4)	5.8 (4)	7.3 (4)	6.4 (4)	19.4 (4)	15.8 (4)	7.9 (7)	9.3 (4)	12.6 (3)	9.7 (3)	9.2 (42)
Vitros Eci			5.6 (3)	7.8 (3)		9.6 (3)	10.2 (5)	6.4 (5)	0.8 (4)	0.9 (4)	1.5 (3)	3.4 (3)	5.1 (33)
Cobas core	10.8 (5)	8.6 (4)	4.7 (6)	5.0 (6)	8.0 (6)	9.9 (6)	24.2 (7)	24.4 (7)	10.2 (7)	8.1 (7)	7.5 (5)	12.3 (6)	11.1 (72)
Elecsys	1.8 (5)	2.3 (6)	6.6 (9)	5.9 (9)	3.8 (11)	5.2 (11)	5.3 (9)	4.9 (9)	5.1 (10)	6.3 (10)	5.1 (11)	5.0 (11)	4.8 (111)
Mean	7.9 (29)	11.9 (25)	6.5 (33)	6.8 (35)	6.9 (34)	8.1 (37)	13.6 (38)	11.5 (38)	6.2 (38)	5.6 (38)	6.6 (37)	7.2 (37)	7.6 (419)
Participant ≥ 3	* Not calculated when numbers of reports were lower than 30												

4. Overall performance

After pilot project completed, the mean MVIS of all participant were calculated as shown in Table 18. The mean MVIS are ranging from 53.0 to 78.0. The overall mean MVIS is 64.4. The MVIS of all markers and trials indicating participating performance were tabulated as shown in Table 19 and were displayed in graphical form as shown in Figure 19. The MVIS of AFP, CA19-9 and β-hCG is constant. The MVIS of PSA, CA125, and CA15-3 is decrease. The MVIS of CEA is increase. Through this survey, roughly sixty percent of participants perform excellence performance in all tumor markers. The tumor marker that most participant performance in an excellence manner, in descending order, is CA15-3 (65.2%), CA125 (62.9%), CEA (61.9%), β-hCG (61.2%), CA19-9 (58.7%), PSA (52.9%), AFP 50.7%) as shown in Figure 20. It is not over 10% of participant need correction for all tumor markers as shown in Table 20 - 23.

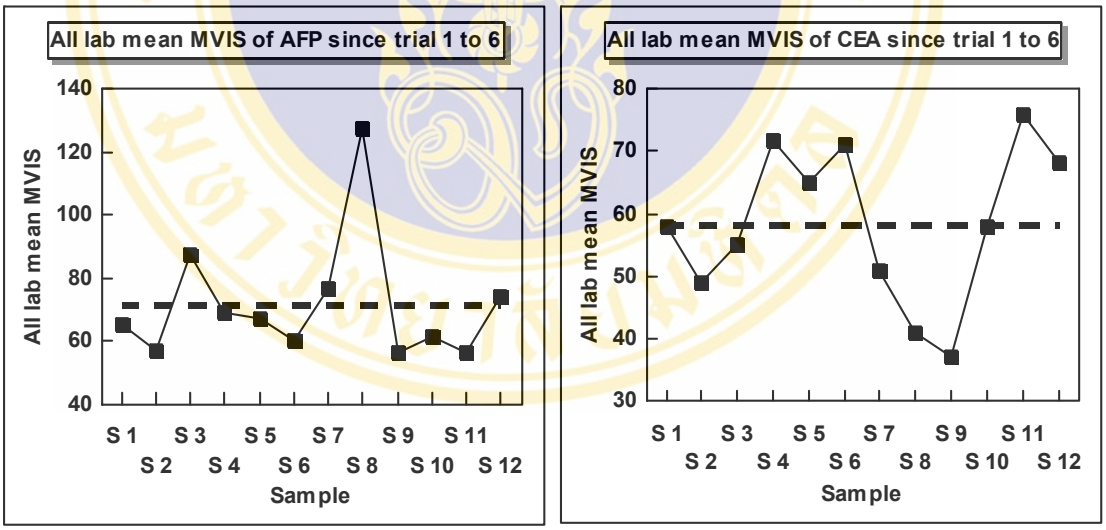

Figure 19. Trend of mean MVIS of tumor markers since trial 1 to 6

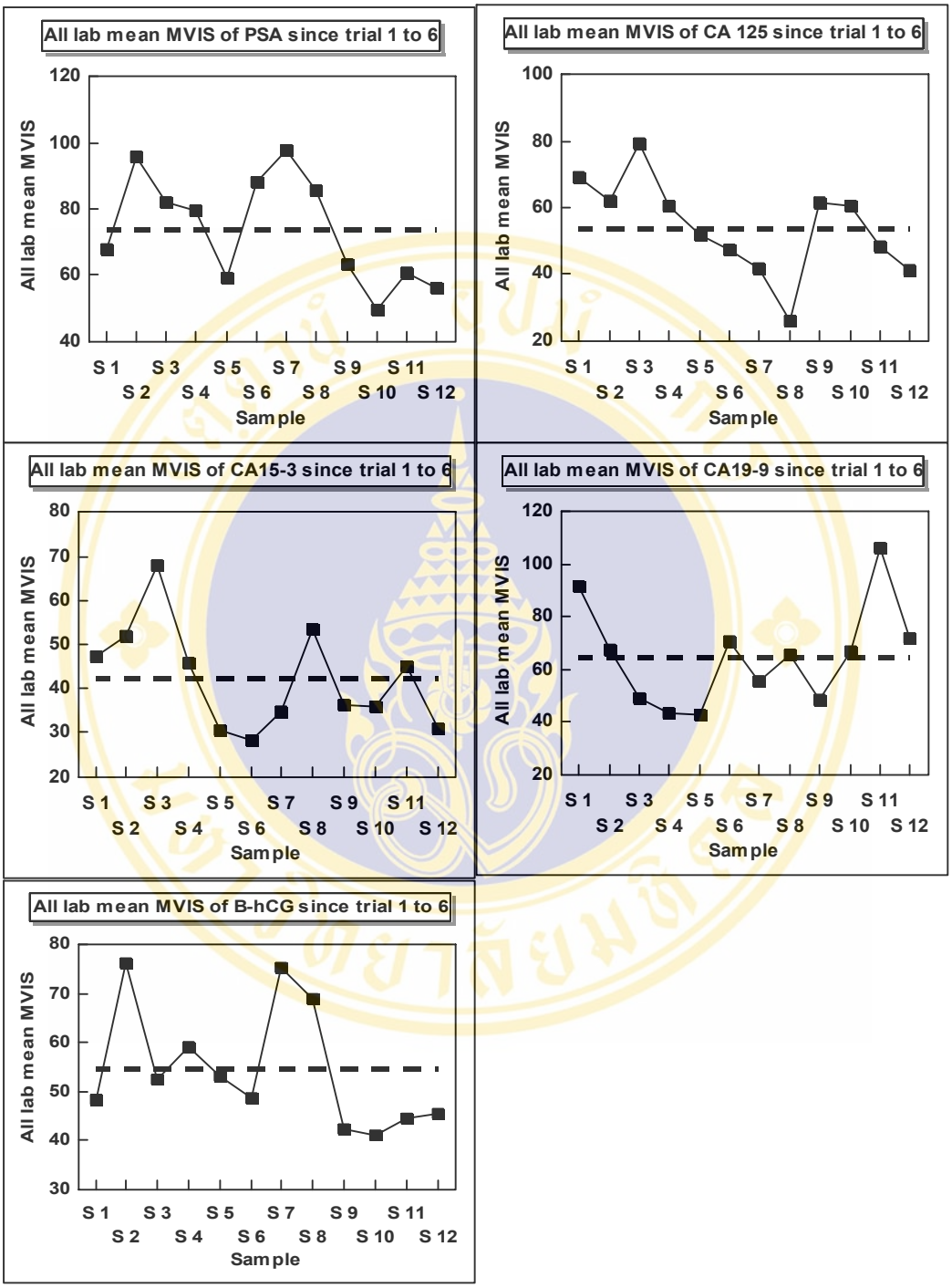

Figure 19. Trend of mean MVIS of tumor markers since trial 1 to 6 (Cont.)

Table 18. Mean MVIS of all participants of this pilot project

Trial	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Trial 6	Mean
Mean MVIS	64.6	69.4	65.7	78.0	53.0	60.0	64.4

Table 19. Mean of MVIS of participant laboratories in pilot project classified by tumor marker

Sample No.	MVIS of sample												Mean
	Trial 1		Trial 2		Trial 3		Trial 4		Trial 5		Trial 6		
	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	S11	S12	
AFP	65.08	57.22	87.49	68.74	67.17	60.42	76.84	127.55	56.07	61.48	56.37	73.91	**71.5**
CEA	57.96	48.94	55.10	71.59	64.95	71.16	51.03	40.97	37.29	58.14	75.81	68.34	**58.4**
PSA	67.98	95.55	82.00	79.52	59.20	88.02	97.76	85.68	63.31	49.44	60.70	55.88	**73.8**
CA125	69.34	61.88	79.26	60.70	51.85	47.04	41.78	25.76	61.27	60.51	48.40	41.32	**54.1**
CA15-3	47.49	52.04	68.03	45.68	30.62	28.39	34.88	53.35	36.31	35.86	44.99	30.85	**42.4**
CA19-9	91.30	67.51	48.94	43.46	42.54	70.94	55.61	65.26	48.26	66.54	106.00	71.88	**64.8**
β-hCG	48.42	76.17	52.55	59.07	53.07	48.48	75.38	69.04	42.41	41.01	44.41	45.47	**54.6**
Mean	63.9	65.6	67.6	61.2	52.8	59.2	61.9	66.8	49.2	53.3	62.4	44.8	**44.8**

Table 20. Number of participant receiving each level of MVIS for AFP and CEA

Result of participating **laboratory**		**Percentages of laboratories each level of MVIS for AFP (number)**					**Percentages of laboratories each level of MVIS for CEA (number)**				
Sample	**Trial**	**Excellence (0 – 50) (n)**	**Good (51 – 100) (n)**	**Medium (101-150) (n)**	**Suspected (151-200) (n)**	**Need correction > 200 (n)**	**Excellence (0 – 50) (n)**	**Good (51 – 100) (n)**	**Medium (101-150) (n)**	**Suspected (151-200) (n)**	**Need correction > 200 (n)**
S 1	1st trial	55.8% (29)	23.1% (12)	13.5% (7)	3.8% (2)	3.8% (2)	57.1% (28)	26.5% (13)	10.2% (5)	4.1% (2)	2.0% (1)
S 2		56.8% (25)	25.0% (11)	13.6% (6)	2.3% (1)	2.3% (1)	67.3% (33)	22.4% (11)	8.2% (4)	0	2.0% (1)
S 3	2nd trial	42.6% (20)	25.5% (12)	12.8% (6)	8.5% (4)	10.6% (5)	67.3% (33)	18.4% (9)	6.1% (3)	4.1% (0)	4.1% (2)
S 4		64.0% (32)	16.0% (8)	10.0% (5)	0	10.0% (5)	43.1% (22)	37.3% (19)	9.8% (5)	5.9% (3)	3.9% (2)
S 5	3rd trial	55.1% (27)	28.6% (14)	8.2% (4)	4.1% (2)	4.1% (2)	61.2% (30)	24.5% (12)	6.1% (3)	2.0% (1)	6.1% (3)
S 6		51.0% (25)	36.7% (18)	8.2% (4)	0	4.1% (2)	59.2% (29)	22.4% (11)	10.2% (5)	0	8.2% (4)
S 7	4th trial	46.0% (23)	16.0% (8)	28.0% (14)	8.0% (4)	2.0% (1)	75.5% (37)	12.2% (6)	6.1% (3)	2.0% (1)	4.1% (2)
S 8		28.6% (14)	20.4% (10)	18.4% (9)	6.1% (3)	26.5% (13)	80.4% (37)	13.0% (6)	2.2% (1)	2.2% (1)	2.2% (1)
S 9	5th trial	51.8% (29)	32.1% (18)	8.9% (5)	7.1% (4)	0	75.5% (40)	14.0% (9)	1.9% (1)	5.77% (3)	0
S 10		48.2% (27)	35.7% (20)	10.7% (6)	1.8% (11)	3.6% (2)	50.9% (27)	34.0% (18)	7.5% (4)	1.9% (1)	5.7% (3)
S 11	6th trial	55.6% (30)	33.3% (18)	9.3% (5)	0	1.3% (1)	48.1% (25)	28.8% (15)	5.8% (3)	7.7% (4)	9.7% (5)
S 12		51.9% (28)	27.8% (15)	9.3% (5)	1.9% (1)	9.3% (5)	59.6% (31)	15.4% (8)	13.5% (7)	3.8% (2)	7.77% (4)
Mean of MVIS		50.7%	26.9%	12.5%	3.6%	6.4%	61.9%	22.8%	7.3%	3.3%	4.7%

Table 21. Number of participant receiving each level of MVIS for PSA and CA125

Result of participating laboratory		Percentages of laboratories each level of MVIS for PSA (number)					Percentages of laboratories each level of MVIS for CA125 (number)				
Sample	**Trial**	**Excellence (0 – 50) (n)**	**Good (51 – 100) (n)**	**Medium (101-150) (n)**	**Suspected (151-200) (n)**	**Need correction > 200 (n)**	**Excellence (0 – 50) (n)**	**Good (51 – 100) (n)**	**Medium (101-150) (n)**	**Suspected (151-200) (n)**	**Need correction > 200 (n)**
S 1	1st trial	60.5% (23)	23.7% (9)	5.3% (2)	0	10.6% (4)	62.5% (10)	12.5% (2)	0	18.8% (3)	6.3% (1)
S 2		50.0% (18)	13.9% (5)	2.8% (1)	5.6% (2)	27.8% (10)	50.0% (8)	25.0% (4)	25.0% (4)	0	0
S 3	2nd trial	41.7% (15)	27.8% (10)	11.1% (4)	16.7% (6)	2.8% (1)	60.0% (9)	13.3% (2)	13.3% (2)	0	13.3% (2)
S 4		48.6% (17)	17.1% (6)	20.0% (7)	5.7% (2)	8.9% (3)	53.3% (8)	33.3% (5)	6.7% (1)	0	6.7% (1)
S 5	3rd trial	67.6% (25)	13.5% (5)	10.8% (4)	2.7% (1)	5.4% (2)	69.2% (9)	23.1% (3)	0	0	7.7% (1)
S 6		47.2% (17)	25.0% (9)	13.9% (5)	2.8% (1)	11.1% (4)	69.2% (9)	23.1% (3)	0	0	7.7% (1)
S 7	4th trial	47.4% (18)	13.2% (5)	21.1% (8)	7.9% (3)	10.5% (4)	57.1% (8)	42.9% (6)	0	0	0
S 8		40.5% (15)	21.6% (8)	21.6% (8)	5.4% (2)	10.8% (4)	57.1% (12)	42.9% (2)	0	0	0
S 9	5th trial	44.2% (19)	34.9% (15)	11.6% (5)	9.3% (4)	0	50.0% (9)	22.2% (4)	22.2% (4)	0	5.6% (1)
S 10		57.1% (24)	33.3% (14)	7.1% (3)	2.4% (1)	0	59.6% (10)	22.2% (4)	11.1% (2)	11.1% (2)	0
S 11	6th trial	60.5% (26)	20.9% (12)	4.8% (2)	0	7.0% (3)	64.7% (11)	17.6% (3)	5.9% (1)	11.8% (2)	0
S 12		66.7% (28)	21.4% (9)	2.4% (1)	2.4% (1)	7.15 (3)	82.4% (14)	5.9% (1)	11.8% (2)	0	0
Mean of MVIS		52.9%	23.1%	10.8%	5.0%	8.2%	62.9%	21.0%	8.6%	3.8%	3.8%

Table 22. Number of participant receiving each level of MVIS for CA15-3 and CA19-9

Result of participating laboratory		Percentages of laboratories each level of MVIS for CA15-3 (number)					Percentages of laboratories each level of MVIS for CA19-9 (number)				
Sample	**Trial**	**Excellence (0 – 50) (n)**	**Good (51 – 100) (n)**	**Medium (101-150) (n)**	**Suspected (151-200) (n)**	**Need correction > 200 (n)**	**Excellence (0 – 50) (n)**	**Good (51 – 100) (n)**	**Medium (101-150) (n)**	**Suspected (151-200) (n)**	**Need correction > 200 (n)**
S 1	1st trial	54.5% (6)	36.4% (4)	0	9.4% (1)	0	31.3% (5)	37.5% (6)	6.3% (1)	6.3% (1)	18.8% (3)
S 2		63.6% (7)	27.3% (3)	9.1% (1)	0	0	42.9% (6)	28.6% (4)	21.4% (3)	0	7.1% (1)
S 3	2nd trial	63.6% (7)	9.1% (1)	18.2% (2)	0	9.1% (1)	78.6% (11)	14.3% (2)	0	0	7.1% (1)
S 4		63.6% (7)	27.3% (3)	9.1% (1)	0	0	78.6% 911)	7.1% (1)	7.1% (1)	7.1% (1)	0
S 5	3rd trial	80.0% (8)	10.0% (1)	10.0% (1)	0	0	69.2% (9)	23.1% (3)	7.0% (1)	0	0
S 6		80.0% (8)	20.0% (2)	0	0	0	53.8% (7)	30.8% (4)	0	7.1% (1)	7.7% (1)
S 7	4th trial	45.5% (5)	54.5% (6)	0	0	0	60.0% (6)	30.0% (3)	0	0	10.0% (1)
S 8		45.5% (5)	54.5% (6)	0	0	0	88.9% (8)	0	0	0	11.1% (1)
S 9	5th trial	76.9% (10)	23.1% (3)	0	0	0	69.2% (9)	15.4% (2)	7.7% (1)	7.8% (1)	0
S 10		76.9% (10)	23.1% (3)	0	0	0	46.2% (6)	38.5% (5)	7.7% (1)	0	7.7% (1)
S 11	6th trial	60.0% (6)	30.0% (3)	10.0% (1)	0	0	38.5% (5)	7.7% (1)	15.4% (2)	23.1% (3)	15.4% (2)
S 12		70.0% (7)	30.0% (3)	0	0	0	61.5% (8)	15.4% (2)	7.7% (1)	7.7% (1)	7.7% (1)
Mean of MVIS		65.2%	28.8%	4.5%	0.8%	0.8%	58.7%	21.3%	7.1%	5.2%	7.7%

Table 23. MVIS and mean of MVIS of participating laboratories in tumor marker scheme

Result of participant laboratory		Percentages of laboratories each level of MVIS for β-hCG (number)				
Sample	**Trial**	**Excellent (0-50) (n)**	**Good (51-100) (n)**	**Medium (101-150) (n)**	**Suspected (151-200) (n)**	**Need correction >200 (n)**
S 1	1st trial	55.9% (19)	32.4% (11)	8.8% (3)	2.9% (1)	0
S 2		48.3% (14)	17.2% (5)	17.2% (5)	10.3% (3)	6.9% (2)
S 3	2nd trial	62.5% (25)	22.5% (9)	12.5% (5)	2.5% (1)	0
S 4		56.1% (23)	29.3% (12)	0	12.2% (5)	2.4% (1)
S 5	3rd trial	65.1% (28)	25.6% (11)	4.7% (2)	2.3% (1)	2.3% (1)
S 6		53.5% (23)	34.9% (15)	9.3% (4)	0	2.3% (1)
S 7	4th trial	46.5% (20)	30.2% (13)	14.0% (6)	2.3% (1)	7.0% (3)
S 8		68.2% (30)	15.9% (7)	6.8% (3)	2.3% (1)	6.8% (3)
S 9	5th trial	36.8% (30)	25.5% (12)	10.6% (5)	0	0
S 10		70.2% (33)	21.3% (10)	6.4% (3)	2.1% (1)	0
S 11	6th trial	69.8% (30)	20.9% (9)	4.7% (2)	4.7% (2)	0
S 12		67.4% (29)	23.3% (10)	7.0% (3)	2.3% (1)	0
Mean of MVIS		61.2%	25.0%	8.2%	3.4%	2.2%

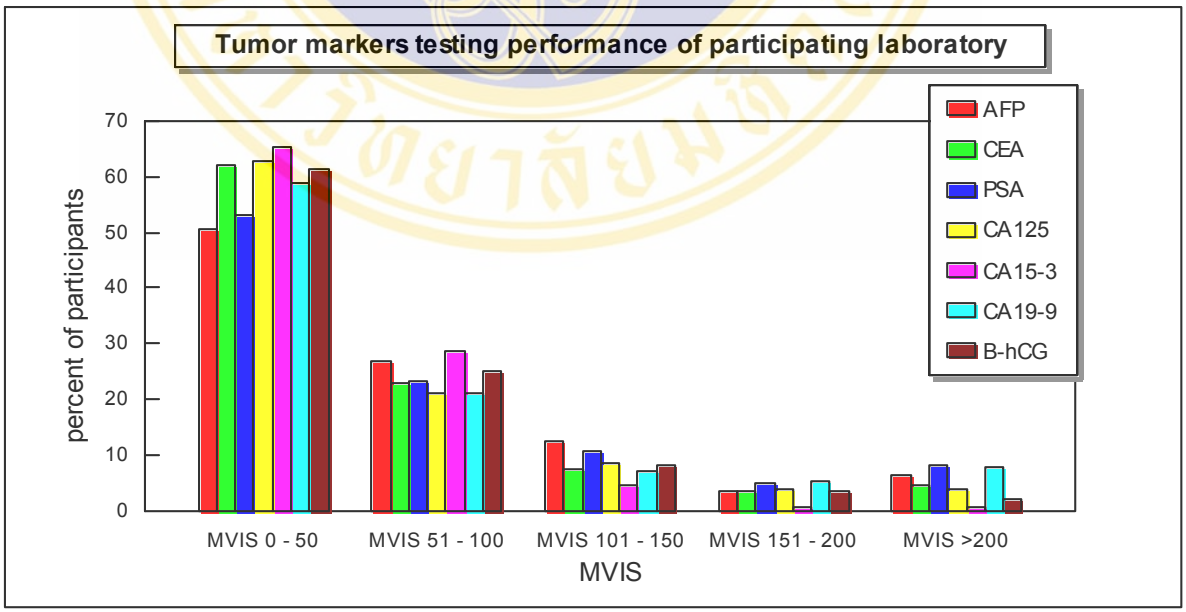

Figure 20. Number of participating laboratories in each category of MVIS of each tumor marker

CHAPTER 6
DISCUSSION

The major component of EQA are participant, having stable control material over the cycle, and reliable data evaluation system. This work showed the pilot study to monitor the tumor marker performance in laboratory service in Thailand by external agency namely external quality assessment scheme in tumor marker (EQAT). There are three approachs to gather the information. Firstly, asking the questions by telephone, secondly, asks the questions directly, and thirdly sending the questionnaires by surface mail and returning after completion. The last approach questionnaire, was designed to discover the need for EQA in tumor marker in our country. The response rate was about thirty percents. This rather low response rate may cause from low numbers of laboratories servicing tumor marker assays. However, 70 laboratory answered to participate in this study, seven out of 70 laboratories (10%) still do not participate any EQAS in tumor marker scheme. Fifty four (79%) of laboratories attended to join our EQAT. From this survey of 70 laboratories, we found tumor markers commonly done, in descending order, were AFP (65 labs, 92.9%), CEA (62 labs, 88.6%), β-hCG (46 labs 65.7%), tPSA (45 labs, 64.3%), CA19-9 (17 labs, 24.3%), CA12-5 (20 labs, 28.6%), CA15-3 (15 labs, 21.4%), and the very rare fPSA (5 labs, 7.1%). The situation was different from the survey of "Hull ands East Yorkshire hospitals NHS Trust" who reported tests commonly done, in descending order, were PSA CEA, CA125, CA19-9, AFP/hCG, and CA15-3 (101). The test survicing depend heavily on the prevalence of cancer in the area. In Thailand, with the high incidence of liver cancer (37.4 / 100 000), AFP assay is the most common test servicing whereas prostate cancer was the most commonly found in foreign country i.e. UK, USA, so PSA assay is the most common test servicing. Among the variety of automate analyzer, the use of Microparticle enzyme immunoassay, Abbott AxSYM, was the most widely used method in UK and Korea in 1995. This was replaced by Chemiluminescence immunoassay analyzer (83).

Study of the quality of liquid and lyophilized control materials found that

contents of liquid form is more similar to human sample; on one hand, lyophilized form is more stable for a long period of time. In this study, lyophilized control serum is stable up to 60 days whereas liquid form is stable only 1 day. The study of stability can be done by many approachs. These approach based varies on advance statistical to simple technique. An example of simple technique is the study of reconstituted serum for the assay of fifteen chemical constitution by Hanok A et al (1968). Moreover, the present study of Lasang P (2003) to stability of control material in hematology still use this technique (102,103). This technique, established the mean of the initial target value and its SD. If there is any value over the ± 2 SD limit, it would be judge as instability. The other one is the technique that investigate the mean rate of change (k) by fitting to the data equation $Y = e^{kt}$ where y is the fraction of initial immunoactivity remaining after time t as the study of hormone stability in human whole blood of Ellis MJ et al (2003); however, the money must be spended to purchase Sigma Stat software from Jandel Scientific, Chicago (104). The other technique, an example of Woodrum et al (1998) to study the stability of PSA. In this technique, the data are require to transformed to a percent recovery from day 0 to standardize the value (105). Afterthat, the general linear modals (GLM) was used to estimate the slope (percent recovery versus time) of the data. The reasonable, reliable, practical statistical method is to use the repeated measures ANOVA. It is the direct technique to study the repeated measure over time. The advantage of this technique is that the part of the error term coming from between subject factor were reduced. Boyanton BL et al (2002) and Jung K et al (1998) introduced this technique in stability studies of routine blood chemistry and PSA respectively (106,107). In this study, effort has been made to use repeated measure is due to nonsupport of manufacturer in this study, unlike the work of Forest JC et al (1998) evaluated the analytical and clinical performance of immunoanalyzer, they took acknowledgement the company for support the reagent and instrument, so repeated measured measure ANOVA can not be used because of the data is insufficient residual degree of freedom (108). In this study, the use of the changes in serial results by RCV was applied (7). It is rely on clinically relevant change. The lyophilized sera and liquid preserved with 0.2% Bronidox was tested as same as the work of Putasiri D (2001) (109). The stability of our liquid serum is limit only on Day 1 as a result of shortage stability of PSA. The most stable tumor marker

in liquid preserved with 0.2% Bronidox is AFP. It is stable up to 20 day. Comparing with the report of Guder WG et al (2002), the stability of PSA in our study of 1 day both 4° C and room temperature is the same as the report at room temperature. At 4° C , The stability of PSA from report of Guder WG et al in 2002 is more stable more than our study up to 30 day. In this study, the stability of AFP, CEA, CA125, CA15-3, β-hCG is longer than the report of Guder WG et al (2002). It is due to the effect of preservative; however, CA19-9 stability in liquid form keeping at 4° C less stable than the report of Guder WG. Surprising, the highest stable of tumor marker control sera of bioref company with sodium azide stabilizer is stable up to 5 years when stored at 4° C - 8° C (110). In contrast, in room temperature, CA19-9 of our study is stable than the report of Guder WG. For PSA, the study at room temperature has the result as the same as Guder WG reported (111). Jung K et al (1998) reported the stability of PSA less than our study that is stable only 4 hours at room temperature (107). Ward AM et al (2001) reported the stability of PSA that is decrease 1.5% per month at 4° C (112). Pikner R et al reported the reduction of PSA is 0.2% per hour at 4° C and –0.21% per hour at room temperature (113). The stability of CA antigen in reported of Banfi G et. Al (1997) is that limit only 1 day keeping at 4° C (114). In UK NEQAS for peptide hormone and related substances, for AFP, CEA, hCG, there are the use of liquid with 0.5% kathon CG-ICP II solution (64). The use of 0.2 μm membrane filter in control sera preparation step and the climate in UK is more cold than Thailand extending the shelf life of control sera; however, its stable is not more than 1 months as implied from the schedule of specimen distribution for AFP, CEA, hCG is every 1 month. In this study only 0.45 μm membrane filter is used in order to saving cost, and the climate is more hot, so the use of lyophilized sera as control material is prefered. The advantage of which is long-term stability. As in report of Chapman D et al (1989), lyophilized sera is stable for 3 years when stored at 2-8 ° C (115). This type of control sera is also used in SEKK, RIQAS and RCPA-AACB.

An EQAT program organized, the data from participant are collected. The ordinary parametric test (mean, SD, %CV) were calculated by in-house programming using Lotus 1-2-3 release 5 in order to saving cost. It is different from the Therapeutic

drug monitoring program in Korea, the statistic evaluation software was purchased from UK (116). There are two formats, descriptive and graphic mode, used for presenting results of our EQAT scheme. In this study, beside ordinary parametric test, consensus value, laboratories BIS, VIS, RBIS, RMVIS and mean of MVIS are reported based on 15% CCV through this study. This scoring system was also used to evaluate performance in EQA scheme in general chemistry in UK. Our established CCV have meaning as same as target coefficients of variation (TCV%), but the quality criteria is different. The %TCV of RIQAS are 12%, 9%, 8%, 12%, 15%, 10% for AFP, CEA, PSA, CA125, CA19-9, β-hCG ,respectively. In UK NEQAS, the CCV for CA125, CA15-3, CA19-9 are 10%, 12.5%, 12.5% of respectively. What the meaning of %TCV or CCV that less than our CCV is that the desirable quality is less rigorous than our study. However, at present, in tumor marker scheme in UK, with exception of CA antigen, the evaluation is changed to rank the results and transformed into their natural logarithm first. The lowest and highest 5% of results are trimmed. The remaining result were calculated for the mean of lab result (ALTM) and the scatter of value (GCV), GLTM, groups of similar method some principle, and MLTM. The cumulative BIAS and its variability (VAR) are reported. The BIS is quite similar as our study. It is the individual result deviated from the target; however, VAR is the GCV of the Bias, not the VIS of our scheme (64). %BIAS and %VAR goal of AFP is 15%, but 20% for CEA and hCG. The CCV is not necessary to use in this evaluation system. Unlucky me, our EQAT scheme can not compare the participating performance with UK NEQAS tumor marker scheme even the CA antigen evaluation use the same evaluation system as our EQAT scheme because their annual review is available only for their participant.

After 1 year implementing of EQAT, the tumor marker performance of participant was monitored. The VIS and %CV usually use in quantitative program. MVIS of AFP, CEA, PSA, CA125, CA15-3, CA19-9, β-hCG is ranging from 127.6 to 56.1, 71.6 to 37.3, 97.8 to 49.4, 79.3 to 25.8, 68.0 to 28.4, 106.0 to 43.5, 76.2 to 42.4 respectively. The narrowest MVIS range is of β-hCG. This is because there is a less variability in β-hCG assay performance. The widest MVIS range is of AFP is widest. This is because the analysis of sample 7 and 8 need pre-dilute sample, so the deviate of result will raise due to pre analytical step included. Dilution performance can be

checked by including in EQA scheme to dilute specimen concentration higher than working range. It is benefit to check whether there is interfering substance such as HAMA. For the mean of MVIS , It is 71.5, 58.4, 73.8, 54.1, 42.4, 64.8, 54.6 for AFP, CEA, PSA, CA125, CA15-3, CA19-9, β-hCG , respectively. The performance of PSA testing is too bad. This is because the low concentration of PSA (around 0.35 ng/ml) since trail 1 to 5. The another reason is due to the organizer fear the participant guessing the concentration of PSA, so the use of seminal fluid as a endogenous substance for the preparation of control samples even Bartos V et al (2003) reported that it is not appropriate introduced because this study don't have any choice to raise up the concentration of PSA due to limitation of high concentration of sera PSA source; however, New York state proficiency test also use it (117,118). As a result of lowest mean of MVIS, the participating performance is best. This is because the consensus value of all instrument is not much difference. For participating performance classified by size, type of hospital, for AFP analysis, less than 120 beds and hospital private hospital perform lowest mean of MVIS of 66.3 and 62.8, respectively. For CEA, PSA, CA15-3 and β-hCG analysis, less than 120 beds and private hospital also perform lowest mean of MVIS of 51.5 and 57.3 for CEA, 56.6 and 69.4 for PSA, 31.8 and 35.1 for CA15-3, 45.0 and 47.0 for β-hCG ,respectively. For CA15-3 and CA19-9, 120 – 500 beds hospital and private hospital perform lowest mean of MVIS of 53.1 and 48.3, 67.6 and 53.1 ,respectively.

The % all lab CV of AFP, CEA, PSA, CA125, CA15-3, CA19-9, β-hCG is 20.7, 26.0, 33.4, 17.9, 14.4, 23.4, 25.2 respectively. The % all lab CV our study is higher than the survey of Austrian EQA system in 1998, Its %CV is 16.2, 7.3, 7.7, 14.0, 9.6, 9.1, 10.5, in the same order of markers (8). By the CAP surveys 2002, The % all lab CV is 12.7, 19.9, 8.4, 20.2, 11.6, 21.8, 22.4 for AFP, CEA, PSA, CA125, CA15-3, CA19-9, β-hCG ,respectively (77). With exception of CA125, the % all lab CV of all markers in Thailand is higher than in CAP surveys. Pilo A et al (1996) reported the between-laboratory variability was 15.2%CV for CA15-3 and 16.0%CV for CA125, and markedly worse 28.3%CV for CA19-9 (11). With exception of CA125, the %CV for CA15-3, CA19-9 is higher than Thailand. The different in %CV of tumor marker testing in Thailand because the less variability of automate analyzer modal in use. Zucchelli GC et al (1997) reported the between-laboratory variability of PSA about

13% (119). It is lower than in Thailand but higher than in Austrian. With exception of surveyed of CA19-9 in Austrian, However, even developed countries such as Austrian, Italy can not meet the CV_A specification stated by Fraser GC (2001). In Thailand, the largest inter-laboratory variation was observed in a group of Abbott AxSYM. It provides highest %CV in PSA, CA125, CA15-3, and CA19-9 in 8, 10, 6, 9 out of 12 samples. Jenny RW et al (2000) reported that air bubbles introduced into the specimen by mixing usually occur in Abbott AxSYM (120). This was confirmed by the CAP surveys 2002 that %CV of Abbott AxSYM is highest for PSA, CA125, CA15-3 of 8.9, 10.8, 8.8 respectively. The second order large inter-laboratory variation is the group of Cobas core. It provides highest %CV in AFP, CEA, and β-hCG in 10, 5, 7 out of 12 sample. This is because Cobas core is a homogeneous enzyme immunoassay which no separation step is necessary. It is less sensitive than heterogeneous assays. The very good instrument is Elecsys. It provides lowest %CV in AFP, CA125, CA15-3, CA19-9, and β-hCG in 5, 9, 6, 9, 5 out of 12 samples. In CAP surveys 2002, Elecsys also provide a good instrument for CA125 analysis. It provide lowest %CV of 4.3. The second order good instrument is Beckman Access. It provides lowest %CV in CEA and PSA in 3, 5 out of 12 samples. By the CAP surveyed in 2002, Beckman Access provided less %CV in PSA and β-hCG of 3.9 and 6.7. Additional, Minividas also provide lowest %CV for CEA in 3 out of 12 samples. In CAP surveyed 2002, the very good instrument is Vitros Eci because it provide lowest %CV for AFP, CEA, and CA15-3 of 3.2, 4.6, 4.9 respectively. This evidence is quite similar in Thailand because it usually provide %CV less than 5. The cause of variability result in Thailand is the use of endogenous substance instead of exogenous substance to spike control sera because this study doesn't test for interference within spiking control sera. Cole LA et al (2004) reported false positive defect with Abbott AxSYM Total β-hCG test due to interfering substance that is the manufacturer responsibility to provide the blocking agent in reagent to solve a problem (121).

Many limitations have been encountered in the organization of EQAT. The first is the limitation of spiking specimen because it is endogenous substance spiking, so it can not calculate exactly desirable concentration. The second factor is a problem concerning the interpretation of laboratory performance because in organizing this pilot project it has been learned that many participants did not taken the dispatched

sample as routine specimens. The third factor is a fee of charge scheme, so it seems that EQAT cost nothing. The participant does not sense of belonging, motivate participant to return result. The fourth matter is that although EQA has been recognized as an educational scheme, the participants do not exploit effectively because many participants would like to know only in what state of quality performance they are in without learning other information provided by scheme and this will limit the continuous improvement of laboratory quality.

There are many reports the ability of EQA for between-laboratory variability reduction. if this scheme is ongoing, it can predict that the between-laboratory variability should be diminished. However, Stern P et al (2003) reported that the inter-laboratory reproducibility improvement was not achieve until the common standard was introduced (81). It was confirmed by the study in UK NEQAS that the %CV was reduced for 15 –20% in the 1990s to less than 10% following introduction of the international standard. Unlike, Clinical chemistry, Immunoassay standardization is less developed because of the lack of pure standards and reference methods (122). The current international standards for tumor markers is limit only for AFP, PSA, hCG, but the standard for CEA is only international reference preparation level. For CA antigen, international standard is not available. In case of international standards are not yet available, as for CEA, it is much more difficult to compare results between method. The method-specific conversion factors required to express ng/ml of CEA in terms of U/L of the international standard for CEA leading different method using difference conversion factors (123). All example above about tumor marker standardization is an example of EQA education. As stated above, it is believe that an EQA can reduce between laboratory variability. If an EQA scheme is ongoing for long time, but the between laboratory variability still high. An organizer will looking for the problems and the way for solving them. An example of high between laboratory variability of tumor marker testing is that each manufacturer use different gradient in their calibrator of hCG assay as known from mutually learning. So , EQA result can motivate the standardization of an assay to provide interchangably among method results. To accomplished that expectation, the multinational EQA and network for rare quantities such as tumor marker, thyroid hormone should be encouraged to make more reliable statistic evaluation. Exchange of experience with other tumor marker scheme, use of

electronic data transmission of results, harmonization on quality goals for the acceptance of EQA results leading us to compare laboratory performance in our country with that others is desirable.

CHAPTER 7
CONCLUSION

The results of this study were concluded as following:

(i) Tumor marker that commonly done, in descending order, AFP (65 labs, 92.9%), CEA (62 labs ,88.6%), β-hCG (46 labs, 65.7%), tPSA 45 labs ,64.3%), CA12-5 (20 labs ,28.6%), CA19-9 (17 labs, 24.3%), CA15-3 (15 labs ,21.4%), and the very rare fPSA (5 labs ,7.1%).

(ii) The automate analyzer that commonly used, in descending order, Abbott AxSYM/IMX 38.4%, Elecsys 30.1%, Cobas Core 8.0%, Minividas 7.9%, Beckman Access 7.3%, Vitros Eci 6.5% and DPC Immulite 1.7%.

(iii) Vitros Eci provide less inter-laboratory variability in AFP (5.7%), Beckman Access for CEA (6.7%) and PSA (5.9%), Vitros Eci for CA125 (3.0%), Minividas for CA15-3 (5.4%), Elecsys CA19-9 (5.5%) and β-hCG (4.8%).

(iv) In Thailand, more than 50 percents of laboratories display an excellent performance in all tumor markers testing; 50.7% for AFP, 61.9% for CEA, 52.9% for PSA, 62.9% for CA125, 65.2% for CA15-3, 58.7% for CA19-9 and 61.2% for β-hCG.

(v) The purposed CCV of tumor marker testing in Thailand is 9.5% for AFP, 8.0% for CEA, 9.2% for PSA, 7.6% for CA125, 7.6% for CA15-3, 8.3% for CA19-9, 7.6% for β-hCG.

(vi) The overall performance of laboratories through this pilot project showing a good performance (mean of MVIS is 64.4), 64.6 in trial 1, 69.4 in trial 2, 65.7 in trial 3, 78.0 in trial 4, 53.0 in trial 5, 60.0 in trial 6.

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APPENDIX

APPENDIX

ผู้วิจัย นายฉัตรชัย มังกรแสงแก้ว นักศึกษาบัณฑิตวิทยาลัย รหัสประจำตัว 4336823MTMT/M
อาจารย์ที่ปรึกษา รองศาสตราจารย์อมรินทร์ ปรีชาวุฒิ
สถานที่ติดต่อ ภาควิชาเคมีคลินิก คณะเทคนิคการแพทย์ มหาวิทยาลัยมหิดล
บางกอกน้อย กรุงเทพฯ 10700
โทรศัพท์ (02) 419-7163

คำชี้แจง โปรดทำเครื่องหมาย √ ลงในช่อง ☐ หรือเติมข้อความลงในช่องว่างที่เว้นไว้ _____
ให้ตรงกับความเป็นจริง

ตอนที่1 ข้อมูลทั่วไป

1.1 ชื่อหน่วยงาน _____เบอร์โทรศัพท์_____
ชื่อหัวหน้าหน่วยงาน_____
ที่อยู่_____

1.2 ชื่อโรงพยาบาล(เฉพาะกรณีสังกัดโรงพยาบาล)_____
โรงพยาบาลมีจำนวนเตียง
☐ น้อยกว่า 120 เตียง ☐ 120-500 เตียง ☐ มากกว่า 500 เตียง

1.3 หน่วยงานของท่านสังกัด
☐ กระทรวงสาธารณสุข ☐ กระทรวงมหาดไทย ☐ กรุงเทพมหานคร
☐ เอกชน ☐ รัฐวิสาหกิจ ☐ กระทรวงกลาโหม
☐ อื่นๆ โปรดระบุ_____

Figure 21A. Questionnaire design page 2

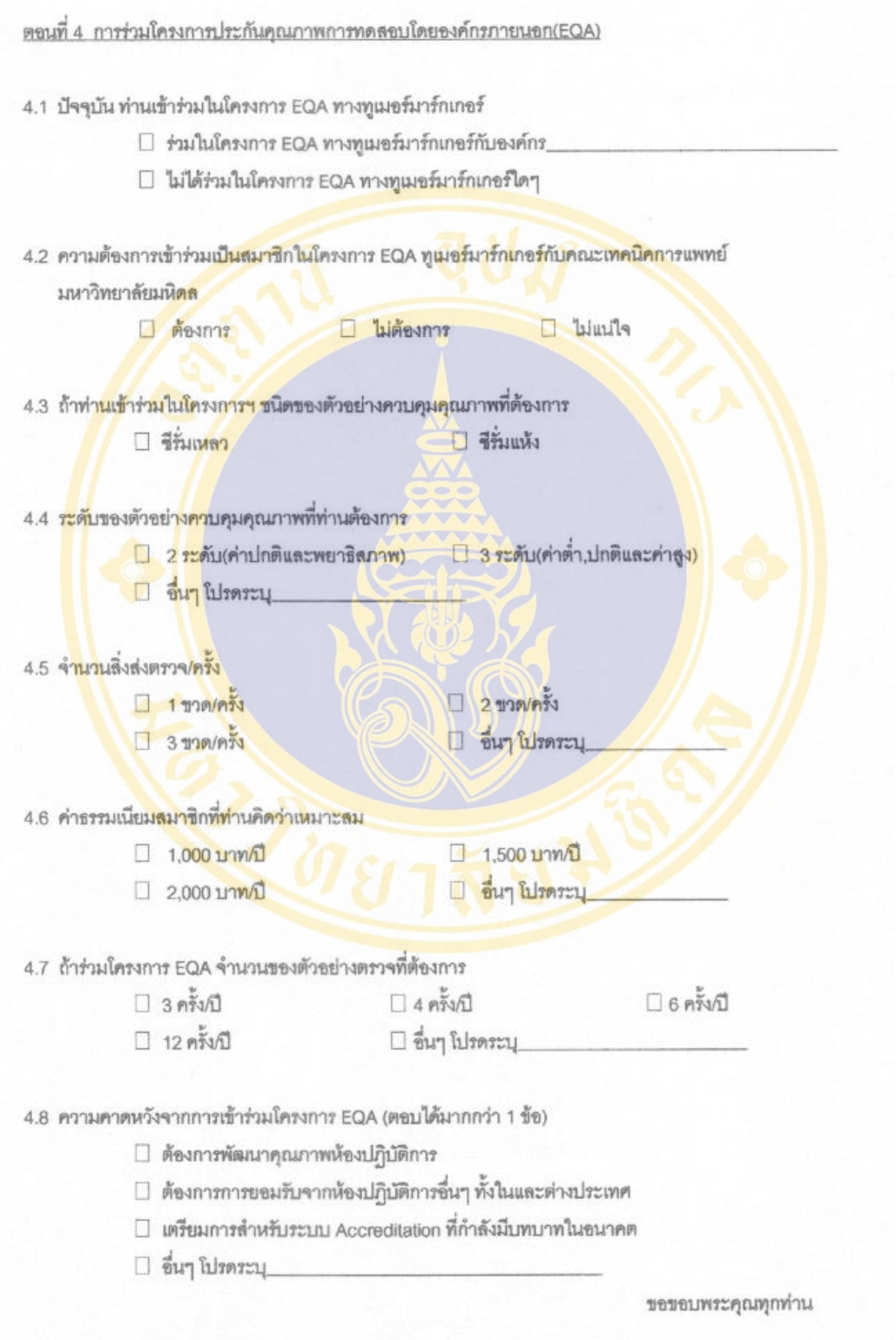
ตอนที่ 2 ข้อมูลการทดสอบทูเมอร์มาร์กเกอร์

คำชี้แจง โปรดทำเครื่องหมาย √ ในช่องว่างให้ตรงกับความเป็นจริง

เครื่องอัตโนมัติที่ใช้ในการตรวจทูเมอร์มาร์กเกอร์(ตอบได้มากกว่า 1 เครื่อง)

	Tumour markers							
	AFP	CEA	tPSA	fPSA	CA 125	CA 15-3	CA 19-9	β-HCG
Abbott AXSYM								
Abbott IMX								
Abbott ARCHITECT								
Bayer ACS Centaur								
Bayer ACS 180								
Bayer immuno 1								
DPC immulite								
DPC immulite 2000								
DPC Coat-a-Count								
BM Elecsys								
BM Enzymun								
Roche Cobas Core								
Beckman Access								
Biomerieux VIDAS								
Wallac Delfia								
Tosoh AIA 600/1200								
Vitros ECI								
ES300/700								
Hybritech Photon Era								
Hybritech Photon II								
Randox ELISA								
Dade Behring Opus								
อื่นๆ โปรดระบุ								

Figure 21B. Questionnaire design page 3



ตอนที่ 4 การร่วมโครงการประกันคุณภาพการทดสอบโดยองค์กรภายนอก(EQA)

4.1 ปัจจุบัน ท่านเข้าร่วมในโครงการ EQA ทางทูเมอร์มาร์กเกอร์

☐ ร่วมในโครงการ EQA ทางทูเมอร์มาร์กเกอร์กับองค์กร_____

☐ ไม่ได้ร่วมในโครงการ EQA ทางทูเมอร์มาร์กเกอร์ใดๆ

4.2 ความต้องการเข้าร่วมเป็นสมาชิกในโครงการ EQA ทูเมอร์มาร์กเกอร์กับคณะเทคนิคการแพทย์ มหาวิทยาลัยมหิดล

☐ ต้องการ ☐ ไม่ต้องการ ☐ ไม่แน่ใจ

4.3 ถ้าท่านเข้าร่วมในโครงการฯ ชนิดของตัวอย่างควบคุมคุณภาพที่ต้องการ

☐ ซีรั่มเหลว ☐ ซีรั่มแห้ง

4.4 ระดับของตัวอย่างควบคุมคุณภาพที่ท่านต้องการ

☐ 2 ระดับ(ค่าปกติและพยาธิสภาพ) ☐ 3 ระดับ(ค่าต่ำ,ปกติและค่าสูง)

☐ อื่นๆ โปรดระบุ_____

4.5 จำนวนสิ่งส่งตรวจ/ครั้ง

☐ 1 ขวด/ครั้ง ☐ 2 ขวด/ครั้ง

☐ 3 ขวด/ครั้ง ☐ อื่นๆ โปรดระบุ_____

4.6 ค่าธรรมเนียมสมาชิกที่ท่านคิดว่าเหมาะสม

☐ 1,000 บาท/ปี ☐ 1,500 บาท/ปี

☐ 2,000 บาท/ปี ☐ อื่นๆ โปรดระบุ_____

4.7 ถ้าร่วมโครงการ EQA จำนวนของตัวอย่างตรวจที่ต้องการ

☐ 3 ครั้ง/ปี ☐ 4 ครั้ง/ปี ☐ 6 ครั้ง/ปี

☐ 12 ครั้ง/ปี ☐ อื่นๆ โปรดระบุ_____

4.8 ความคาดหวังจากการเข้าร่วมโครงการ EQA (ตอบได้มากกว่า 1 ข้อ)

☐ ต้องการพัฒนาคุณภาพห้องปฏิบัติการ

☐ ต้องการการยอมรับจากห้องปฏิบัติการอื่นๆ ทั้งในและต่างประเทศ

☐ เตรียมการสำหรับระบบ Accreditation ที่กำลังมีบทบาทในอนาคต

☐ อื่นๆ โปรดระบุ_____

ขอขอบพระคุณทุกท่าน

Figure 21C. Questionnaire design page 5

Table 24. AFP assayed (ng/ml) at various time intervals of two forms control material (lyophilized and liquid) after stored at 4° C and room temperature

Day	Control material 1				Control material 2			
	Liquid form 1		Lyophilized form 1		Liquid form 2		Lyophilized form 2	
	4 ° C	RT	4 ° C	RT	4 ° C	RT	4 ° C	RT
Day 0	14.35	14.35	14.35	14.35	2.21	2.21	2.21	2.21
Day 1	14.81	15.81	14.95	13.99	2.25	2.27	2.27	2.08
Day 5	15.28	16.14	14.20	13.82	2.28	2.43	2.41	2.18
Day 7	16.78	17.37	15.70	14.13	2.52	2.47	2.23	2.36
Day 10	16.23	16.35	14.46	13.17	2.43	2.66	2.32	2.12
Day 15	14.91	15.22	14.68	14.08	2.23	2.36	2.03	2.11
Day 20	14.60	18.01	13.24	13.58	2.39	2.24	2.00	1.96
Day 30	12.66	22.11*	12.06	11.68	1.95	2.06	1.88	1.82
Day 45	12.57	20.20	14.08	14.69	1.82	2.87	2.13	2.21
Day 60	15.38	17.17	15.21	14.63	2.41	3.28	2.41	2.32
Mean	14.76	17.27	14.29	13.81	2.25	2.48	2.09	2.14
SD	1.03	2.35	1.03	0.88	0.22	0.36	0.18	0.16
%CV	7.22	16.58	7.22	6.36	0.70	14.65	8.11	7.51

* Result deviated from target value at day 0 greater than calculated RCV of AFP = 50%

Table 25. CEA assayed (ng/ml) at various time intervals of two forms control material (lyophilized and liquid) after stored at 4° C and room temperature

Day	Control material 1				Control material 2			
	Liquid form 1		Lyophilized form 1		Liquid form 2		Lyophilized form 2	
	4 ° C	RT	4 ° C	RT	4 ° C	RT	4 ° C	RT
Day 0	1.8	1.8	1.8	1.8	2.1	2.1	2.1	2.1
Day 1	1.9	2.0	2.1	1.6	2.2	2.3	2.2	1.8
Day 5	1.9	2.1	1.9	1.6	2.2	2.1	2.0	1.9
Day 7	2.0	2.0	1.7	1.8	2.1	2.4	1.9	1.9
Day 10	1.8	2.0	1.7	1.8	2.1	2.0	2.0	2.0
Day 15	2.0	3.0*	1.7	1.8	2.0	2.5	1.9	1.9
Day 20	2.1	6.7*	1.9	1.7	2.1	2.8*	1.9	1.9
Day 30	2.3	12.4*	2.0	1.7	2.3	2.9*	2.0	2.1
Day 45	2.4	7.3*	2.1	2.2	2.6	4.0*	2.1	2.2
Day 60	2.6*	6.5*	2.3	2.3	2.8*	6.3*	2.6	2.7
Mean	2.08	4.58	1.92	1.83	2.25	2.94	2.07	2.05
SD	0.27	3.54	0.20	0.24	0.26	1.32	0.21	0.26
%CV	12.86	77.33	10.57	12.87	11.48	44.97	10.20	11.48

* Result deviated from target value at day 0 greater than calculated RCV of CEA = 35.3%

Table 26. PSA assayed (ng/ml) at various time intervals of two forms control material (lyophilized and liquid) after stored at 4° C and room temperature

Day	Control material 1				Control material 2			
	Liquid form 1		Lyophilized form 1		Liquid form 2		Lyophilized form 2	
	4 ° C	RT	4 ° C	RT	4 ° C	RT	4 ° C	RT
Day 0	16.38	16.38	16.38	16.38	26.29	26.29	26.29	26.29
Day 1	14.46	12.31	14.89	15.13	19.42	19.42	23.83	25.91
Day 5	12.22	9.81	14.72	14.94	15.21*	15.21*	25.12	23.10
Day 7	11.04	7.98*	16.14	15.73	12.44*	12.44*	25.06	26.52
Day 10	12.04	7.76*	15.25	16.17	12.66*	12.66*	26.03	25.99
Day 15	11.54	7.17*	15.90	14.98	9.91*	9.91*	24.32	25.19
Day 20	11.13	7.37*	14.94	16.43	8.32*	8.32*	25.12	23.22
Day 30	10.69	10.83	13.91	13.50	3.71*	3.71*	22.65	22.42
Day 45	9.38*	6.13*	15.59	14.65	9.14*	9.14*	22.57	22.32
Day 60	9.85	4.90*	15.44	14.91	***	***	25.41	24.17
Mean	11.87	18.84	15.32	15.28	18.84	13.01	24.65	24.51
SD	2.11	3.36	0.74	0.91	3.36	6.67	1.28	1.66
%CV	17.87	17.84	4.82	5.96	17.84	51.26	5.20	6.77

* Result deviated from target value at day 0 greater than calculated RCV of PSA = 42.0%

*** Abbott AxSYM cann't analyzed sample

Table 27. CA125 assayed (U/ml) at various time intervals of two forms control material (lyophilized and liquid) after stored at 4° C and room temperature

Day	Control material 1				Control material 2			
	Liquid form 1		Lyophilized form 1		Liquid form 2		Lyophilized form 2	
	4 ° C	RT	4 ° C	RT	4 ° C	RT	4 ° C	RT
Day 0	10.98	10.98	10.98	10.98	11.29	11.29	11.29	11.29
Day 1	12.71	11.97	11.86	11.72	11.31	11.99	13.36	10.10
Day 5	12.72	14.04	10.88	12.06	11.08	13.61	11.47	11.00
Day 7	14.38	12.20	10.88	10.52	12.86	12.36	10.02	12.39
Day 10	12.49	14.10	8.30	11.84	10.01	13.02	10.37	9.65
Day 15	8.65	16.22	9.89	9.50	10.79	11.20	8.88	9.26
Day 20	12.07	31.17*	8.11	7.75	8.53	13.24	8.80	8.65
Day 30	9.91	107.14*	9.53	8.87	10.28	22.35	6.59	10.31
Day 45	10.14	89.18*	10.14	9.15	9.71	***	8.33	9.32
Day 60	9.63	***	9.13	9.79	11.65	***	8.42	9.55
Mean	11.37	34.11	10.00	10.22	10.75	13.63	9.75	10.15
SD	1.78	37.09	1.23	1.44	1.19	3.63	1.95	1.13
%CV	15.69	108.72	12.30	14.11	11.07	26.62	20.00	11.09

* Result deviated from target value at day 0 greater than calculated RCV of CA125 = 141.5%

*** Abbott AxSYM cann't analyzed sample

Table 28. CA15-3 assayed (U/ml) at various time intervals of two forms control material (lyophilized and liquid) after stored at 4° C and room temperature

Day	Control material 1				Control material 2			
	Liquid form 1		Lyophilized form 1		Liquid form 2		Lyophilized form 2	
	4 ° C	RT	4 ° C	RT	4 ° C	RT	4 ° C	RT
Day 0	10.1	10.1	10.1	10.1	10.6	10.6	10.6	10.6
Day 1	9.9	10.1	9.4	9.1	10.6	9.8	9.3	9.5
Day 5	10.0	9.8	8.7	8.8	10.3	10.2	9.6	9.1
Day 7	9.6	10.2	9.2	9.6	10.4	10.5	9.5	9.5
Day 10	9.7	9.7	9.5	8.8	10.1	10.7	10.0	10.0
Day 15	10.3	10.7	8.8	9.3	10.9	10.5	8.3	8.7
Day 20	10.1	11.1	9.0	8.7	10.3	10.4	9.0	9.2
Day 30	10.0	8.9	9.2	9.4	10.1	10.6	9.7	10.3
Day 45	10.1	7.7*	8.2	8.0	8.7	10.4	8.3	8.8
Day 60	9.6	10.8	9.5	10.0	10.8	1.4*	9.8	10.2
Mean	9.95	9.91	9.16	9.28	10.28	9.51	9.41	9.59
SD	0.24	1.00	0.53	0.65	0.62	2.86	0.72	0.66
%CV	2.43	10.06	5.75	7.05	6.01	30.08	7.67	6.85

* Result deviated from target value at day 0 greater than calculated RCV of CA15-3 = 21.2%

Table 29. CA19-9 assayed (U/ml) at various time intervals of two forms control material (lyophilized and liquid) after stored at 4° C and room temperature

Day	Control material 1				Control material 2			
	Liquid form 1		Lyophilized form 1		Liquid form 2		Lyophilized form 2	
	4 ° C	RT	4 ° C	RT	4 ° C	RT	4 ° C	RT
Day 0	5.44	5.44	5.44	5.44	7.82	7.82	7.82	7.82
Day 1	6.06	5.87	5.23	5.72	7.99	8.52	7.66	8.89
Day 5	5.53	4.92	5.10	4.44	8.29	8.81	7.95	8.08
Day 7	5.07	4.70	5.15	5.45	8.58	8.69	7.84	8.11
Day 10	4.35	5.70	4.56	4.68	8.29	9.95	7.99	7.78
Day 15	4.61	8.95	4.78	6.76	7.65	8.77	6.14	7.44
Day 20	3.92	25.48*	5.19	3.57	6.60	7.97	8.20	8.12
Day 30	3.88	81.57*	4.75	4.35	6.94	8.52	5.87	7.75
Day 45	5.10	65.12*	4.06	3.80	7.49	22.31*	6.84	7.81
Day 60	3.94	43.40*	5.05	5.60	8.22	***	10.85	8.84
Mean	4.79	25.12	4.93	4.98	7.79	10.15	7.72	8.06
SD	0.77	28.56	0.40	0.98	0.63	4.60	1.37	0.47
%CV	16.01	113.73	8.16	19.73	8.12	45.31	17.75	5.82

* Result deviated from target value at day 0 greater than calculated RCV of CA19-9 = 70.4%

*** Abbott AxSYM cann't analyzed sample

Table 30. β-hCG assayed (mIU/ml) at various time intervals of two forms control material (lyophilized and liquid) after stored at 4° C and room temperature

Day	Control material 1				Control material 2			
	Liquid form 1		Lyophilized form 1		Liquid form 2		Lyophilized form 2	
	4 ° C	RT	4 ° C	RT	4 ° C	RT	4 ° C	RT
Day 0	19.88	19.88	19.88	19.88	539.07	539.07	539.07	539.07
Day 1	23.25	22.93	21.79	20.57	640.58	651.96	599.72	586.78
Day 5	23.00	21.69	22.03	20.95	638.91	614.42	582.76	565.69
Day 7	20.49	20.41	21.27	21.29	612.08	606.75	565.51	554.35
Day 10	20.42	20.17	20.87	20.78	631.94	557.16	547.38	546.06
Day 15	20.05	22.10	20.03	20.30	595.44	550.83	531.39	540.49
Day 20	21.03	102.09*	20.31	19.15	567.60	531.78	550.01	508.71
Day 30	17.29	171.29*	17.16	18.76	490.65	57.38*	492.67	502.22
Day 45	16.72	129.79*	18.31	16.99	491.21	472.26	474.40	480.91
Day 60	19.35	***	20.34	19.91	569.91	***	540.68	537.51
Mean	20.15	59.00	20.20	19.86	577.74	509.07	542.36	536.18
SD	1.51	59.37	1.51	1.28	56.62	177.45	37.66	31.36
%CV	7.46	100.63	7.46	6.44	9.80	34.86	6.94	5.85

* Result deviated from target value at day 0 greater than calculated RCV of β-hCG = 50%

*** Abbott AxSYM cann't analyzed sample

Table 31. Analysis of liquid form 1 concentration before and after mailing

Parameter		Chiang Mai	Khon Kaen	Songklar	Chonburi	Rachaburi	Bangkok
AFP (ng/ml)	Before	17.14	14.10	14.33	15.15	14.42	16.38
	After	16.09	14.08	13.19	14.22	15.73	16.03
CEA (ng/ml)	Before	2.3	4.2*	2.8	4.3*	2.6	2.1
	After	2.1	2.4*	2.4*	2.3*	2.5	2.2
PSA (ng/ml)	Before	6.85*	5.56*	5.55*	3.41*	5.55*	7.74*
	After	8.72*	6.76*	6.77*	5.82*	7.08*	8.44*
CA125 (U/ml)	Before	16.36	17.80	15.72	20.66	21.21	13.26
	After	13.09	16.89	11.95	14.33	14.52	13.55
CA15-3 (U/ml)	Before	10.1	3.1*	11.3	1.7*	11.2	9.6
	After	9.9	11.8*	10.6	9.5*	11.1	10.3
CA19-9 (U/ml)	Before	5.89	0.00*	2.30*	0.00*	6.71	5.52
	After	5.28	2.23*	5.86*	5.95*	5.11	4.83
β-hCG (mIU/ml)	Before	20.21	19.83	20.64	14.90	7.36*	20.00
	After	21.22	21.39	20.75	19.38	22.01*	20.91
Mailing time (day)		8	13	13	15	12	5

* Result deviated from target value at day 0 greater than calculated RCV of AFP = 50%, CEA = 33.5%, PSA = 42.0%, CA125 = 141.5%, CA15-3 = 21.2%, CA19-9 = 70.4%, β-hCG = 50%

Table 32 Analysis of liquid form 2 concentration before and after mailing

Parameter		Chiang Mai	Khon Kaen	Songklar	Chonburi	Rachaburi	Bangkok
AFP (ng/ml)	Before	2.35	1.99	2.55	2.47	2.36	2.24
	After	2.57	2.22	2.25	2.52	2.38	2.39
CEA (ng/ml)	Before	2.3	2.4	3.0	4.0*	2.5	2.3
	After	2.6	2.4	2.4	2.5*	2.5	2.2
PSA (ng/ml)	Before	10.17*	8.13*	6.80*	8.58*	8.64*	11.30*
	After	12.77*	10.35*	10.00*	9.63*	11.41*	13.45*
CA125 (U/ml)	Before	13.81	11.35	23.11	19.11	12.93	11.78
	After	12.96	11.22	11.39	13.90	15.54	12.68
CA15-3 (U/ml)	Before	9.7	10.9	11.6	3.4*	10.8	10.0
	After	9.6	10.7	11.1	9.9*	11.6	9.8
CA19-9 (U/ml)	Before	9.03	9.01	9.48	0.00	8.89	7.99
	After	11.45	8.72	7.87	9.46	8.58	8.76
β-hCG (mIU/ml)	Before	558.32	523.56	128.53*	526.45	532.67	598.25
	After	592.51	535.96	531.14*	551.08	591.25	627.92
Mailing time (day)		8	13	13	15	12	5

* Result deviated from target value at day 0 greater than calculated RCV of AFP = 50%, CEA = 33.5%, PSA = 42.0%, CA125 = 141.5%, CA15-3 = 21.2%, CA19-9 = 70.4%, β-hCG = 50%

Table 33. Analysis of lyophilized form 1 concentration before and after mailing

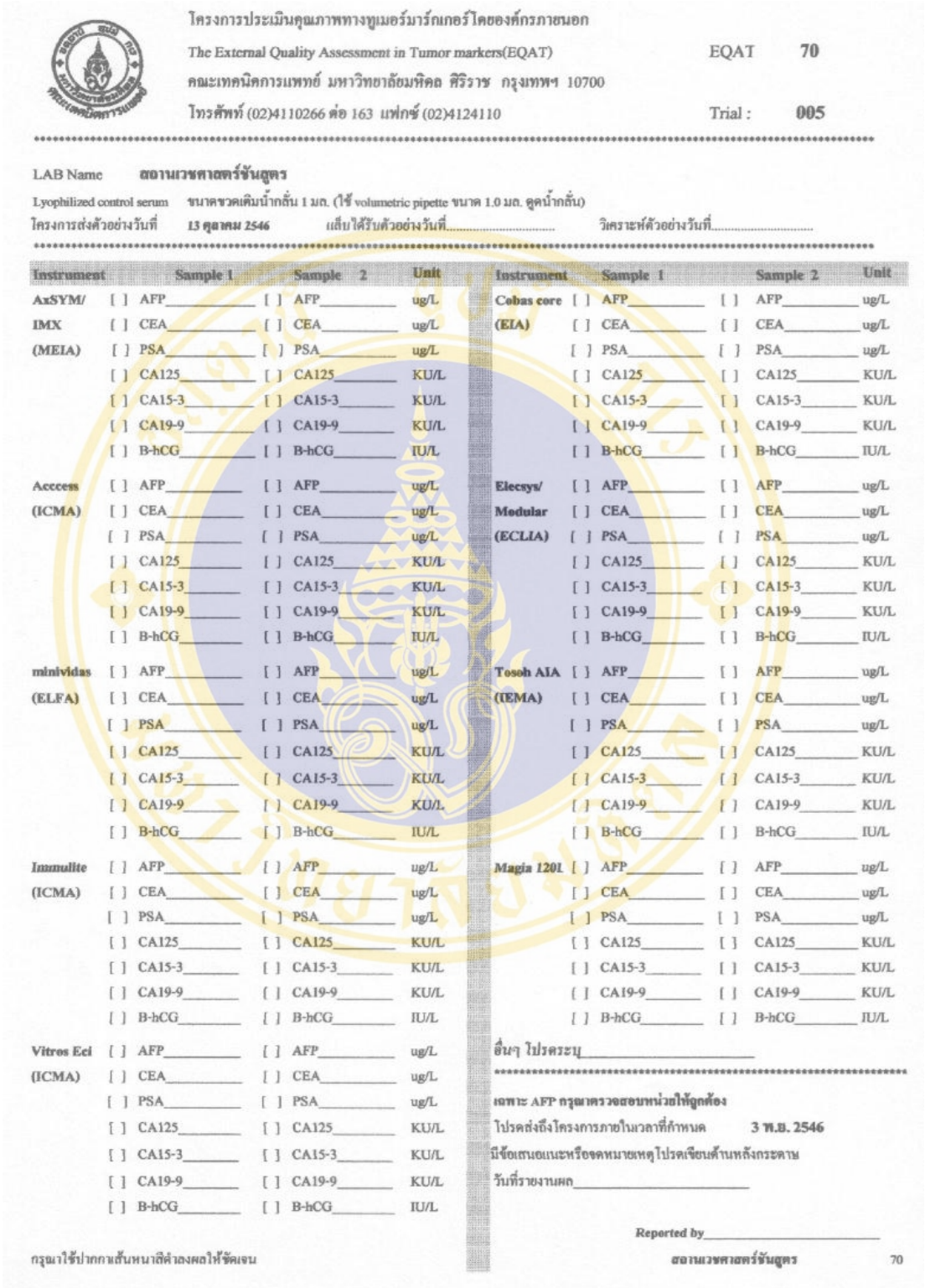
Parameter		Chiang Mai	Khon Kaen	Songklar	Chonburi	Racahburi	Bangkok
AFP (ng/ml)	Before	13.30	13.22	14.63	13.12	14.75	12.73
	After	13.99	13.87	13.30	14.48	14.75	14.31
CEA (ng/ml)	Before	1.7	1.6	1.8	1.8	1.9	1.9
	After	1.6	1.77	1.9	1.8	1.8	1.8
PSA (ng/ml)	Before	14.78	14.00	15.52	15.39	15.56	14.25
	After	14.90	13.98	15.54	15.44	14.81	14.07
CA125 (U/ml)	Before	9.93	10.05	9.58	10.07	11.42	10.24
	After	11.20	10.79	10.95	9.92	11.25	10.12
CA15-3 (U/ml)	Before	9.5	9.4	10.1	9.7	8.9	8.8
	After	9.9	10.0	10.1	9.6	8.9	8.7
CA19-9 (U/ml)	Before	5.36	4.25	4.90	5.17	5.08	5.13
	After	5.88	4.42	4.60	4.68	5.32	4.74
β-hCG (mIU/ml)	Before	10.27	18.95	21.47	21.13	20.98	20.77
	After	19.67	19.67	19.46	19.46	21.10	19.54
Mailing time (day)		12	12	12	11	7	4

* Result deviated from target value at day 0 greater than calculated RCV of AFP = 50%, CEA = 33.5%, PSA = 42.0%, CA125 = 141.5%, CA15-3 = 21.2%, CA19-9 = 70.4%, β-hCG = 50%

Table 34. Analysis of lyophilized form 2 concentration before and after mailing

Parameter		Chiang Mai	Khon Kaen	Songklar	Chonburi	Rachaburi	Bangkok
AFP (ng/ml)	Before	2.02	2.05	2.04	2.18	2.30	2.11
	After	2.00	2.06	1.97	2.19	2.32	2.10
CEA (ng/ml)	Before	2.0	1.8	1.7	2.1	2.2	1.9
	After	1.8	1.8	1.8	1.8	2.0	1.9
PSA (ng/ml)	Before	23.10	23.12	24.09	25.86	26.01	24.36
	After	23.46	22.39	23.42	25.16	25.23	24.29
CA125 (U/ml)	Before	10.67	8.49	9.60	10.75	11.77	10.73
	After	11.78	10.44	9.16	10.91	12.20	11.14
CA15-3 (U/ml)	Before	10.4	10.2	9.8	9.8	10.7	9.0
	After	9.9	10.8	10.1	9.7	10.4	9.3
CA19-9 (U/ml)	Before	6.74	6.93	8.27	8.18	15.15	7.68
	After	6.90	7.62	7.53	7.56	9.02	8.48
β-hCG (mIU/ml)	Before	517.60	525.69	492.37	545.58	560.355	592.06
	After	522.49	519.04	510.99	557.34	564.17	577.95
Mailing time (day)		12	12	12	11	7	4

* Result deviated from target value at day 0 greater than calculated RCV of AFP = 50%, CEA = 33.5%, PSA = 42.0%, CA125 = 141.5%, CA15-3 = 21.2%, CA19-9 = 70.4%, β-hCG = 50%



โครงการประเมินคุณภาพทางทูเมอร์มาร์กเกอร์โดยองค์กรภายนอก

The External Quality Assessment in Tumor markers(EQAT) EQAT **70**

คณะเทคนิคการแพทย์ มหาวิทยาลัยมหิดล ศิริราช กรุงเทพฯ 10700

โทรศัพท์ (02)4110266 ต่อ 163 แฟกซ์ (02)4124110 Trial : **005**

LAB Name **สถานเวชศาสตร์ชันสูตร**

Lyophilized control serum ขนาดขวดเติมน้ำกลั่น 1 มล. (ใช้ volumetric pipette ขนาด 1.0 มล. ดูดน้ำกลั่น)

โครงการส่งตัวอย่างวันที่ **13 ตุลาคม 2546** เลี้ยงได้รับตัวอย่างวันที่..... วิเคราะห์ตัวอย่างวันที่.....

Instrument		Sample 1		Sample 2	Unit
AxSYM/	[ ]	AFP	[ ]	AFP	ug/L
IMX	[ ]	CEA	[ ]	CEA	ug/L
(MEIA)	[ ]	PSA	[ ]	PSA	ug/L
	[ ]	CA125	[ ]	CA125	KU/L
	[ ]	CA15-3	[ ]	CA15-3	KU/L
	[ ]	CA19-9	[ ]	CA19-9	KU/L
	[ ]	B-hCG	[ ]	B-hCG	IU/L
Acccess	[ ]	AFP	[ ]	AFP	ug/L
(ICMA)	[ ]	CEA	[ ]	CEA	ug/L
	[ ]	PSA	[ ]	PSA	ug/L
	[ ]	CA125	[ ]	CA125	KU/L
	[ ]	CA15-3	[ ]	CA15-3	KU/L
	[ ]	CA19-9	[ ]	CA19-9	KU/L
	[ ]	B-hCG	[ ]	B-hCG	IU/L
minividas	[ ]	AFP	[ ]	AFP	ug/L
(ELFA)	[ ]	CEA	[ ]	CEA	ug/L
	[ ]	PSA	[ ]	PSA	ug/L
	[ ]	CA125	[ ]	CA125	KU/L
	[ ]	CA15-3	[ ]	CA15-3	KU/L
	[ ]	CA19-9	[ ]	CA19-9	KU/L
	[ ]	B-hCG	[ ]	B-hCG	IU/L
Immulite	[ ]	AFP	[ ]	AFP	ug/L
(ICMA)	[ ]	CEA	[ ]	CEA	ug/L
	[ ]	PSA	[ ]	PSA	ug/L
	[ ]	CA125	[ ]	CA125	KU/L
	[ ]	CA15-3	[ ]	CA15-3	KU/L
	[ ]	CA19-9	[ ]	CA19-9	KU/L
	[ ]	B-hCG	[ ]	B-hCG	IU/L
Vitros Eci	[ ]	AFP	[ ]	AFP	ug/L
(ICMA)	[ ]	CEA	[ ]	CEA	ug/L
	[ ]	PSA	[ ]	PSA	ug/L
	[ ]	CA125	[ ]	CA125	KU/L
	[ ]	CA15-3	[ ]	CA15-3	KU/L
	[ ]	CA19-9	[ ]	CA19-9	KU/L
	[ ]	B-hCG	[ ]	B-hCG	IU/L

Instrument		Sample 1		Sample 2	Unit
Cobas core	[ ]	AFP	[ ]	AFP	ug/L
(EIA)	[ ]	CEA	[ ]	CEA	ug/L
	[ ]	PSA	[ ]	PSA	ug/L
	[ ]	CA125	[ ]	CA125	KU/L
	[ ]	CA15-3	[ ]	CA15-3	KU/L
	[ ]	CA19-9	[ ]	CA19-9	KU/L
	[ ]	B-hCG	[ ]	B-hCG	IU/L
Elecsys/	[ ]	AFP	[ ]	AFP	ug/L
Modular	[ ]	CEA	[ ]	CEA	ug/L
(ECLIA)	[ ]	PSA	[ ]	PSA	ug/L
	[ ]	CA125	[ ]	CA125	KU/L
	[ ]	CA15-3	[ ]	CA15-3	KU/L
	[ ]	CA19-9	[ ]	CA19-9	KU/L
	[ ]	B-hCG	[ ]	B-hCG	IU/L
Tosoh AIA	[ ]	AFP	[ ]	AFP	ug/L
(IEMA)	[ ]	CEA	[ ]	CEA	ug/L
	[ ]	PSA	[ ]	PSA	ug/L
	[ ]	CA125	[ ]	CA125	KU/L
	[ ]	CA15-3	[ ]	CA15-3	KU/L
	[ ]	CA19-9	[ ]	CA19-9	KU/L
	[ ]	B-hCG	[ ]	B-hCG	IU/L
Magia 1201	[ ]	AFP	[ ]	AFP	ug/L
	[ ]	CEA	[ ]	CEA	ug/L
	[ ]	PSA	[ ]	PSA	ug/L
	[ ]	CA125	[ ]	CA125	KU/L
	[ ]	CA15-3	[ ]	CA15-3	KU/L
	[ ]	CA19-9	[ ]	CA19-9	KU/L
	[ ]	B-hCG	[ ]	B-hCG	IU/L

อื่นๆ โปรดระบุ_____

เฉพาะ AFP กรุณาตรวจสอบหน่วยให้ถูกต้อง

โปรดส่งถึงโครงการภายในเวลาที่กำหนด **3 พ.ย. 2546**

มีข้อเสนอแนะหรือจดหมายเหตุโปรดเขียนด้านหลังกระดาษ

วันที่รายงานผล_____

*Reported by*_____

สถานเวชศาสตร์ชันสูตร 70

กรุณาใช้ปากกาเส้นหนาสีดำลงผลให้ชัดเจน

Figure 22. Request form

Page 1

โครงการประเมินคุณภาพทางห้องปฏิบัติการโดยวัดจากภายนอก

The National External Quality Assessment in Tumor markers(NEQAT)

N EQAT

Lab. Name : สถาบันวิทยบริการจุฬาฯ Lab code : 70 Trial : 004

Analyte	Instrument	Sample	Your result	Your Group Result (outlier exclusion)			BIS	Yours VIS	Q	All lab MVIS	Acceptable range Lower limit	Acceptable range Upper limit	Total n	CCV
unit				n	Mean	SD	%CV							
AFP		1											15	
kU/l		2											15	
CEA		1											15	
ug/l		2											15	
PSA		1											15	
ug/l		2											15	
CA 125		1											15	
kU/l		2											15	
CA 15-3		1											15	
kU/l		2											15	
CA 19-9		1											15	
kU/l		2											15	
B-hCG		1											15	
IU/l		2											15	

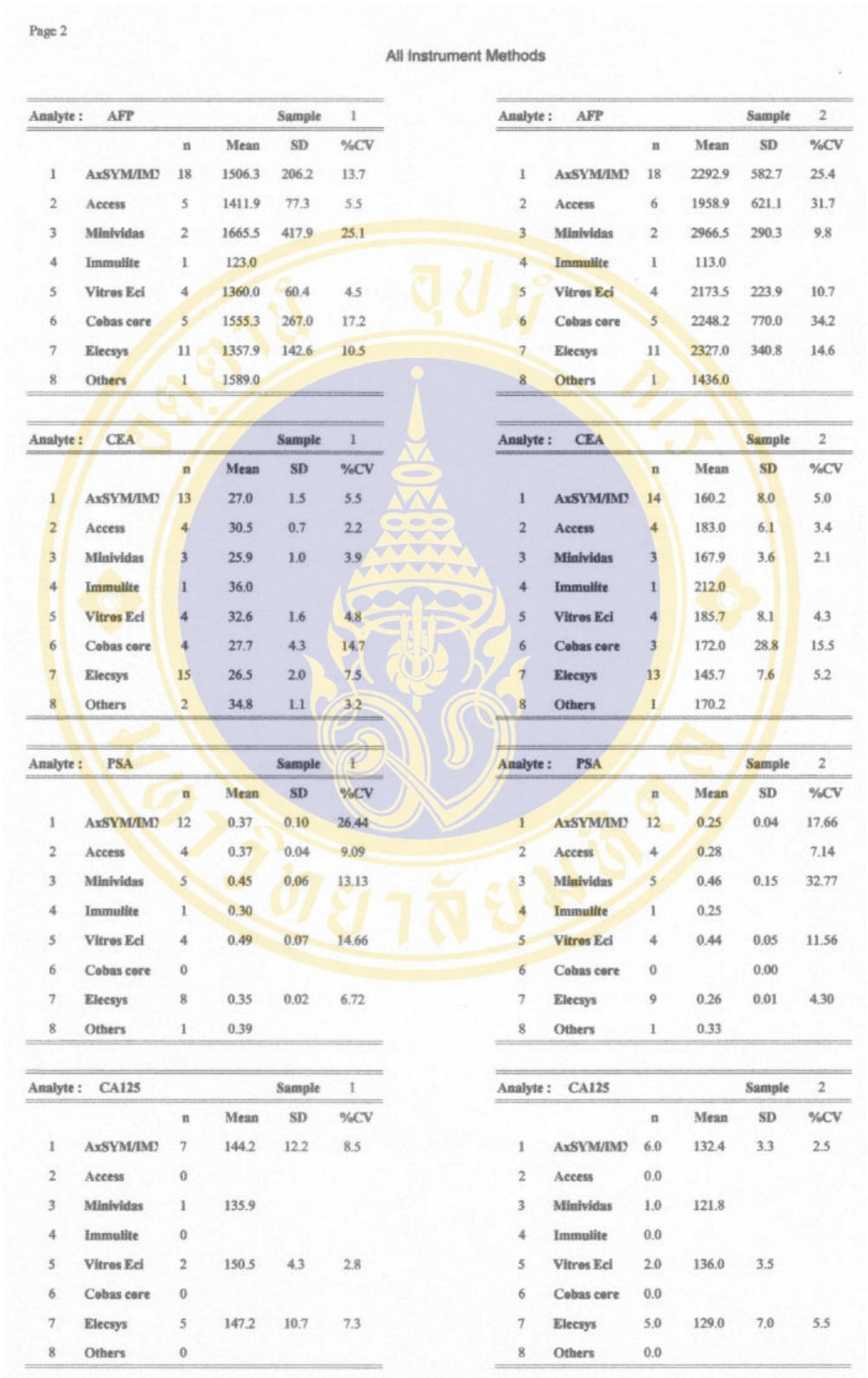
Evaluated date 12 ส.ค. 46
16:21:01

Mean Variance Index Score (MVIS) ==> [redacted] <== Your QA Grade

Num Test : 0

Mean MVIS of all participants is ==> 99.1

Figure 23A. Assessment report form page 1



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All Instrument Methods

Analyte : AFP				Sample 1	
		n	Mean	SD	%CV
1	AxSYM/IMX	18	1506.3	206.2	13.7
2	Access	5	1411.9	77.3	5.5
3	Minividas	2	1665.5	417.9	25.1
4	Immulite	1	123.0		
5	Vitros Eci	4	1360.0	60.4	4.5
6	Cobas core	5	1555.3	267.0	17.2
7	Elecsys	11	1357.9	142.6	10.5
8	Others	1	1589.0		

Analyte : AFP				Sample 2	
		n	Mean	SD	%CV
1	AxSYM/IMX	18	2292.9	582.7	25.4
2	Access	6	1958.9	621.1	31.7
3	Minividas	2	2966.5	290.3	9.8
4	Immulite	1	113.0		
5	Vitros Eci	4	2173.5	223.9	10.7
6	Cobas core	5	2248.2	770.0	34.2
7	Elecsys	11	2327.0	340.8	14.6
8	Others	1	1436.0		

Analyte : CEA				Sample 1	
		n	Mean	SD	%CV
1	AxSYM/IMX	13	27.0	1.5	5.5
2	Access	4	30.5	0.7	2.2
3	Minividas	3	25.9	1.0	3.9
4	Immulite	1	36.0		
5	Vitros Eci	4	32.6	1.6	4.8
6	Cobas core	4	27.7	4.3	14.7
7	Elecsys	15	26.5	2.0	7.5
8	Others	2	34.8	1.1	3.2

Analyte : CEA				Sample 2	
		n	Mean	SD	%CV
1	AxSYM/IMX	14	160.2	8.0	5.0
2	Access	4	183.0	6.1	3.4
3	Minividas	3	167.9	3.6	2.1
4	Immulite	1	212.0		
5	Vitros Eci	4	185.7	8.1	4.3
6	Cobas core	3	172.0	28.8	15.5
7	Elecsys	13	145.7	7.6	5.2
8	Others	1	170.2		

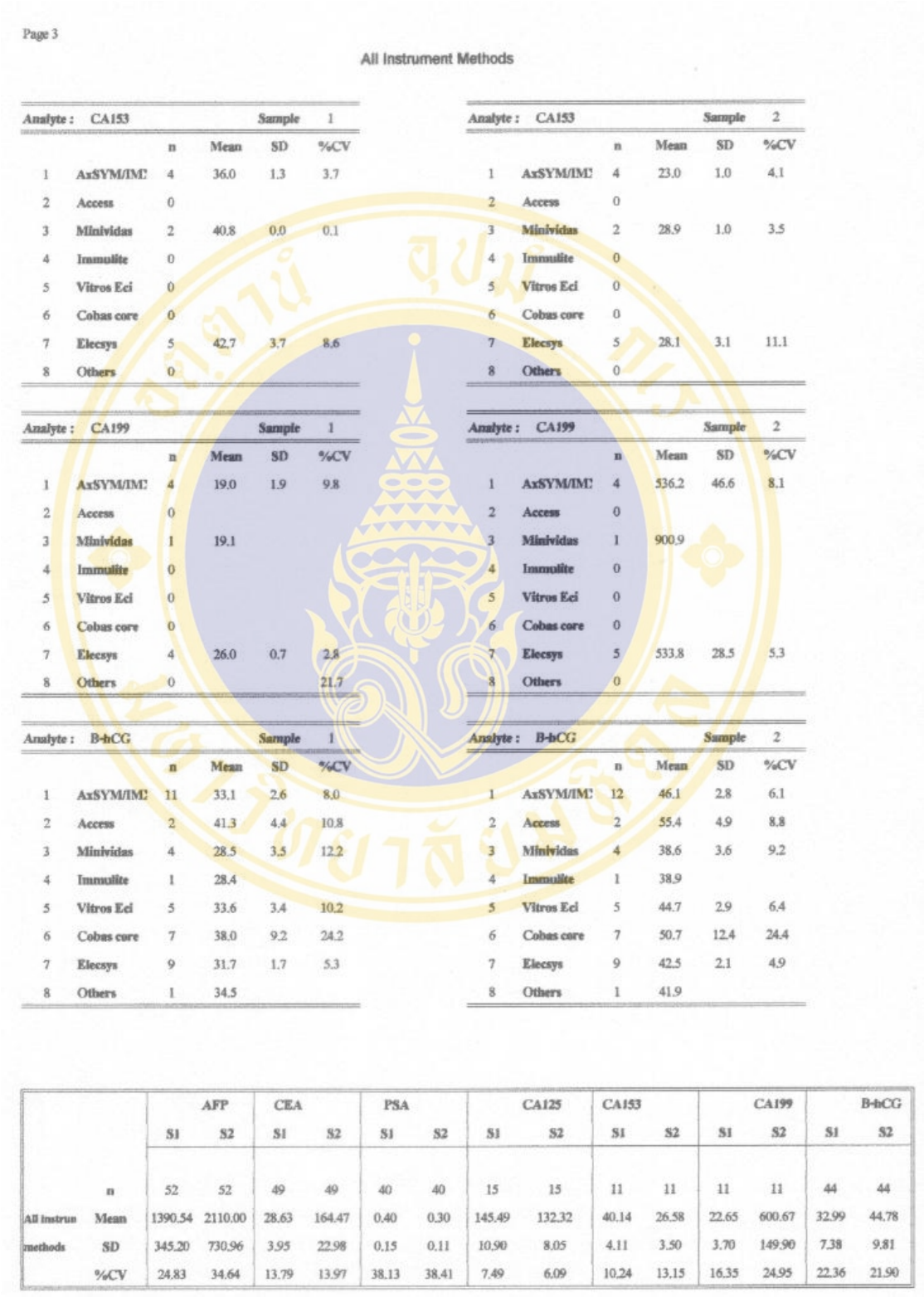
Analyte : PSA				Sample 1	
		n	Mean	SD	%CV
1	AxSYM/IMX	12	0.37	0.10	26.44
2	Access	4	0.37	0.04	9.09
3	Minividas	5	0.45	0.06	13.13
4	Immulite	1	0.30		
5	Vitros Eci	4	0.49	0.07	14.66
6	Cobas core	0			
7	Elecsys	8	0.35	0.02	6.72
8	Others	1	0.39		

Analyte : PSA				Sample 2	
		n	Mean	SD	%CV
1	AxSYM/IMX	12	0.25	0.04	17.66
2	Access	4	0.28		7.14
3	Minividas	5	0.46	0.15	32.77
4	Immulite	1	0.25		
5	Vitros Eci	4	0.44	0.05	11.56
6	Cobas core	0		0.00	
7	Elecsys	9	0.26	0.01	4.30
8	Others	1	0.33		

Analyte : CA125				Sample 1	
		n	Mean	SD	%CV
1	AxSYM/IMX	7	144.2	12.2	8.5
2	Access	0			
3	Minividas	1	135.9		
4	Immulite	0			
5	Vitros Eci	2	150.5	4.3	2.8
6	Cobas core	0			
7	Elecsys	5	147.2	10.7	7.3
8	Others	0			

Analyte : CA125				Sample 2	
		n	Mean	SD	%CV
1	AxSYM/IMX	6.0	132.4	3.3	2.5
2	Access	0.0			
3	Minividas	1.0	121.8		
4	Immulite	0.0			
5	Vitros Eci	2.0	136.0	3.5	
6	Cobas core	0.0			
7	Elecsys	5.0	129.0	7.0	5.5
8	Others	0.0			

Figure 23B. Assessment report form page 2



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All Instrument Methods

Analyte : CA153				Sample 1	
		n	Mean	SD	%CV
1	AxSYM/IMI	4	36.0	1.3	3.7
2	Access	0			
3	Minividas	2	40.8	0.0	0.1
4	Immulite	0			
5	Vitros Eci	0			
6	Cobas core	0			
7	Elecsys	5	42.7	3.7	8.6
8	Others	0			

Analyte : CA153				Sample 2	
		n	Mean	SD	%CV
1	AxSYM/IMI	4	23.0	1.0	4.1
2	Access	0			
3	Minividas	2	28.9	1.0	3.5
4	Immulite	0			
5	Vitros Eci	0			
6	Cobas core	0			
7	Elecsys	5	28.1	3.1	11.1
8	Others	0			

Analyte : CA199				Sample 1	
		n	Mean	SD	%CV
1	AxSYM/IMI	4	19.0	1.9	9.8
2	Access	0			
3	Minividas	1	19.1		
4	Immulite	0			
5	Vitros Eci	0			
6	Cobas core	0			
7	Elecsys	4	26.0	0.7	2.8
8	Others	0			21.7

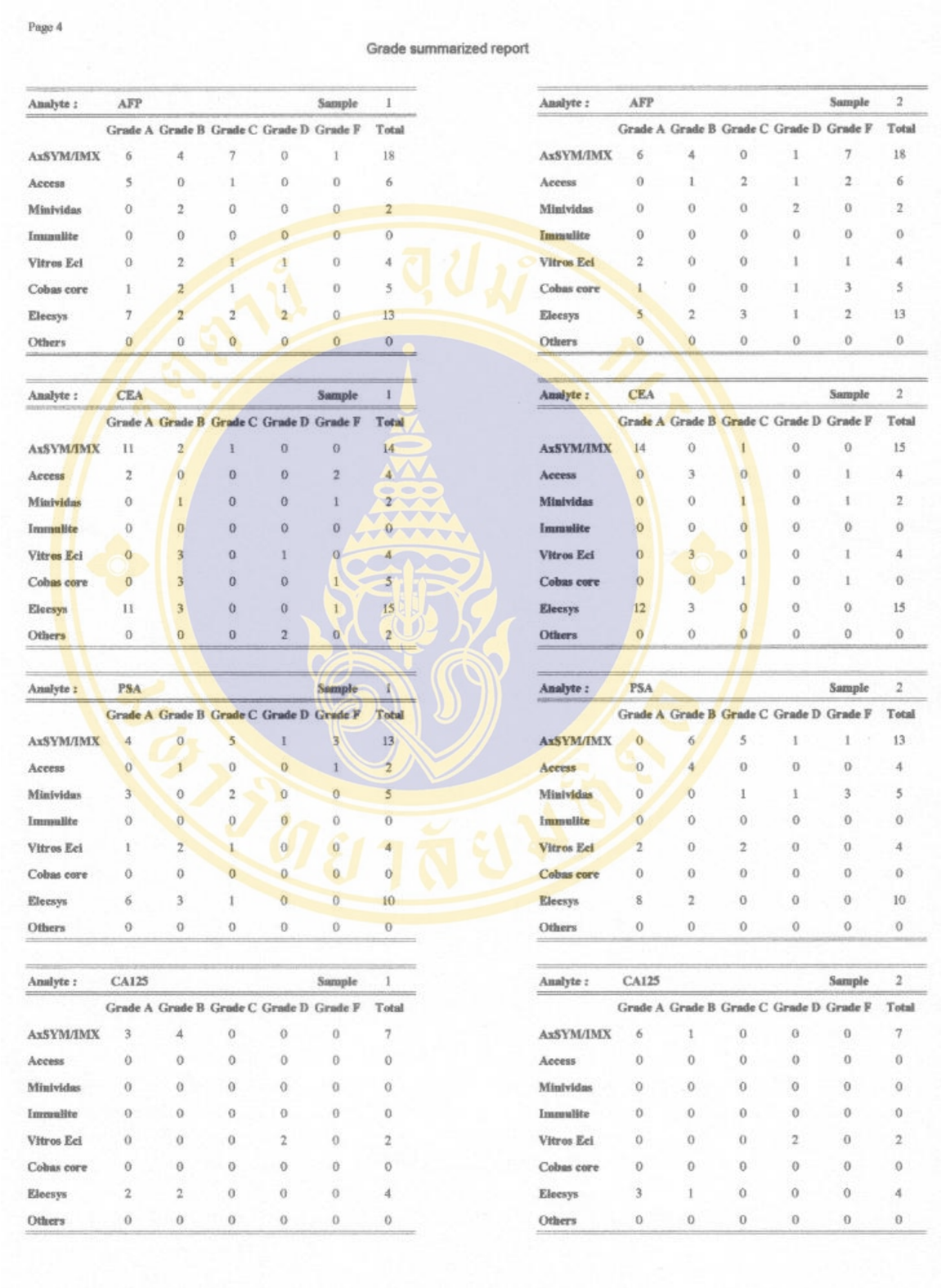
Analyte : CA199				Sample 2	
		n	Mean	SD	%CV
1	AxSYM/IMI	4	536.2	46.6	8.1
2	Access	0			
3	Minividas	1	900.9		
4	Immulite	0			
5	Vitros Eci	0			
6	Cobas core	0			
7	Elecsys	5	533.8	28.5	5.3
8	Others	0			

Analyte : B-hCG				Sample 1	
		n	Mean	SD	%CV
1	AxSYM/IMI	11	33.1	2.6	8.0
2	Access	2	41.3	4.4	10.8
3	Minividas	4	28.5	3.5	12.2
4	Immulite	1	28.4		
5	Vitros Eci	5	33.6	3.4	10.2
6	Cobas core	7	38.0	9.2	24.2
7	Elecsys	9	31.7	1.7	5.3
8	Others	1	34.5		

Analyte : B-hCG				Sample 2	
		n	Mean	SD	%CV
1	AxSYM/IMI	12	46.1	2.8	6.1
2	Access	2	55.4	4.9	8.8
3	Minividas	4	38.6	3.6	9.2
4	Immulite	1	38.9		
5	Vitros Eci	5	44.7	2.9	6.4
6	Cobas core	7	50.7	12.4	24.4
7	Elecsys	9	42.5	2.1	4.9
8	Others	1	41.9		

		AFP		CEA		PSA		CA125		CA153		CA199		B-hCG	
		S1	S2	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2	S1	S2
	n	52	52	49	49	40	40	15	15	11	11	11	11	44	44
All instrun	Mean	1390.54	2110.00	28.63	164.47	0.40	0.30	145.49	132.32	40.14	26.58	22.65	600.67	32.99	44.78
methods	SD	345.20	730.96	3.95	22.98	0.15	0.11	10.90	8.05	4.11	3.50	3.70	149.90	7.38	9.81
	%CV	24.83	34.64	13.79	13.97	38.13	38.41	7.49	6.09	10.24	13.15	16.35	24.95	22.36	21.90

Figure 23C. Assessment report form page 3



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Grade summarized report

Analyte :	AFP				Sample	1
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	6	4	7	0	1	18
Access	5	0	1	0	0	6
Minividas	0	2	0	0	0	2
Immulite	0	0	0	0	0	0
Vitros Eci	0	2	1	1	0	4
Cobas core	1	2	1	1	0	5
Elecsys	7	2	2	2	0	13
Others	0	0	0	0	0	0

Analyte :	AFP				Sample	2
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	6	4	0	1	7	18
Access	0	1	2	1	2	6
Minividas	0	0	0	2	0	2
Immulite	0	0	0	0	0	0
Vitros Eci	2	0	0	1	1	4
Cobas core	1	0	0	1	3	5
Elecsys	5	2	3	1	2	13
Others	0	0	0	0	0	0

Analyte :	CEA				Sample	1
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	11	2	1	0	0	14
Access	2	0	0	0	2	4
Minividas	0	1	0	0	1	2
Immulite	0	0	0	0	0	0
Vitros Eci	0	3	0	1	0	4
Cobas core	0	3	0	0	1	5
Elecsys	11	3	0	0	1	15
Others	0	0	0	2	0	2

Analyte :	CEA				Sample	2
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	14	0	1	0	0	15
Access	0	3	0	0	1	4
Minividas	0	0	1	0	1	2
Immulite	0	0	0	0	0	0
Vitros Eci	0	3	0	0	1	4
Cobas core	0	0	1	0	1	0
Elecsys	12	3	0	0	0	15
Others	0	0	0	0	0	0

Analyte :	PSA				Sample	1
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	4	0	5	1	3	13
Access	0	1	0	0	1	2
Minividas	3	0	2	0	0	5
Immulite	0	0	0	0	0	0
Vitros Eci	1	2	1	0	0	4
Cobas core	0	0	0	0	0	0
Elecsys	6	3	1	0	0	10
Others	0	0	0	0	0	0

Analyte :	PSA				Sample	2
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	0	6	5	1	1	13
Access	0	4	0	0	0	4
Minividas	0	0	1	1	3	5
Immulite	0	0	0	0	0	0
Vitros Eci	2	0	2	0	0	4
Cobas core	0	0	0	0	0	0
Elecsys	8	2	0	0	0	10
Others	0	0	0	0	0	0

Analyte :	CA125				Sample	1
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	3	4	0	0	0	7
Access	0	0	0	0	0	0
Minividas	0	0	0	0	0	0
Immulite	0	0	0	0	0	0
Vitros Eci	0	0	0	2	0	2
Cobas core	0	0	0	0	0	0
Elecsys	2	2	0	0	0	4
Others	0	0	0	0	0	0

Analyte :	CA125				Sample	2
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	6	1	0	0	0	7
Access	0	0	0	0	0	0
Minividas	0	0	0	0	0	0
Immulite	0	0	0	0	0	0
Vitros Eci	0	0	0	2	0	2
Cobas core	0	0	0	0	0	0
Elecsys	3	1	0	0	0	4
Others	0	0	0	0	0	0

Figure 23D. Assessment report form page 4

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Grade summarized report

Analyte :	CA153					Sample 1
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	2	0	0	1	1	4
Access	0	0	0	0	0	0
Minividas	0	0	0	2	0	2
Immulite	0	0	0	0	0	0
Vitros Eci	0	0	0	0	0	0
Cobas core	0	0	0	0	0	0
Elecsys	1	3	0	0	0	4
Others	0	0	0	0	0	0

Analyte :	CA153					Sample 2
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	2	0	0	1	1	4
Access	0	0	0	0	0	0
Minividas	0	0	0	2	0	2
Immulite	0	0	0	0	0	0
Vitros Eci	0	0	0	0	0	0
Cobas core	0	0	0	0	0	0
Elecsys	0	4	0	0	0	4
Others	0	0	0	0	0	0

Analyte :	CA199					Sample 1
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	2	1	1	0	1	5
Access	0	0	0	0	0	0
Minividas	0	0	0	0	0	0
Immulite	0	0	0	0	0	0
Vitros Eci	0	0	0	0	0	0
Cobas core	0	0	0	0	0	0
Elecsys	2	0	1	0	1	4
Others	0	0	0	0	0	0

Analyte :	CA199					Sample 2
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	2	1	0	0	0	0
Access	0	0	0	0	0	0
Minividas	0	0	0	0	0	0
Immulite	0	0	0	0	0	0
Vitros Eci	0	0	0	0	0	0
Cobas core	0	0	0	0	0	0
Elecsys	4	0	0	0	0	4
Others	0	0	0	0	0	0

Analyte :	B-hCG					Sample 1
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	5	7	0	0	0	13
Access	0	0	0	1	1	2
Minividas	0	2	1	0	1	4
Immulite	0	0	0	0	0	0
Vitros Eci	2	2	1	0	0	5
Cobas core	2	2	1	0	3	8
Elecsys	8	2	0	0	0	10
Others	0	0	0	0	0	0

Analyte :	B-hCG					Sample 2
	Grade A	Grade B	Grade C	Grade D	Grade F	Total
AxSYM/IMX	10	3	0	0	0	13
Access	0	0	0	0	2	2
Minividas	0	2	0	1	1	4
Immulite	0	0	0	0	0	0
Vitros Eci	5	0	0	0	0	5
Cobas core	2	2	1	0	3	8
Elecsys	9	0	0	1	0	10
Others	0	0	0	0	0	0

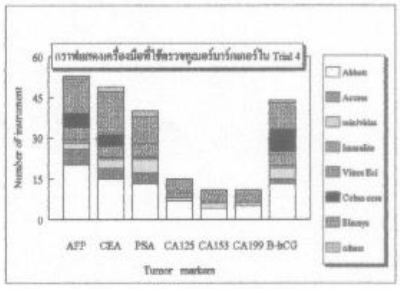

Figure 23E. Assessment report form page 5

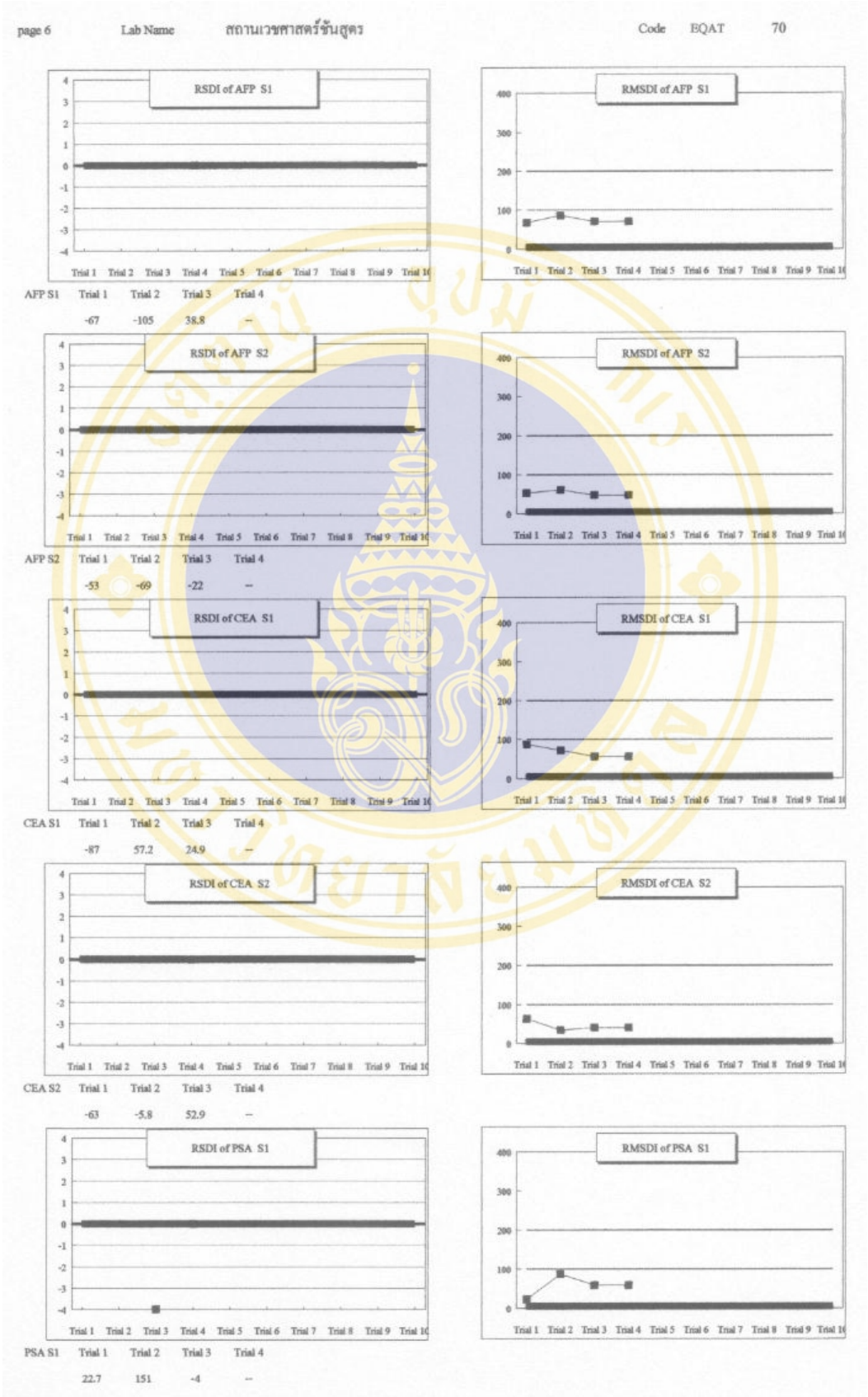

Figure 23F. Assessment report form page 6

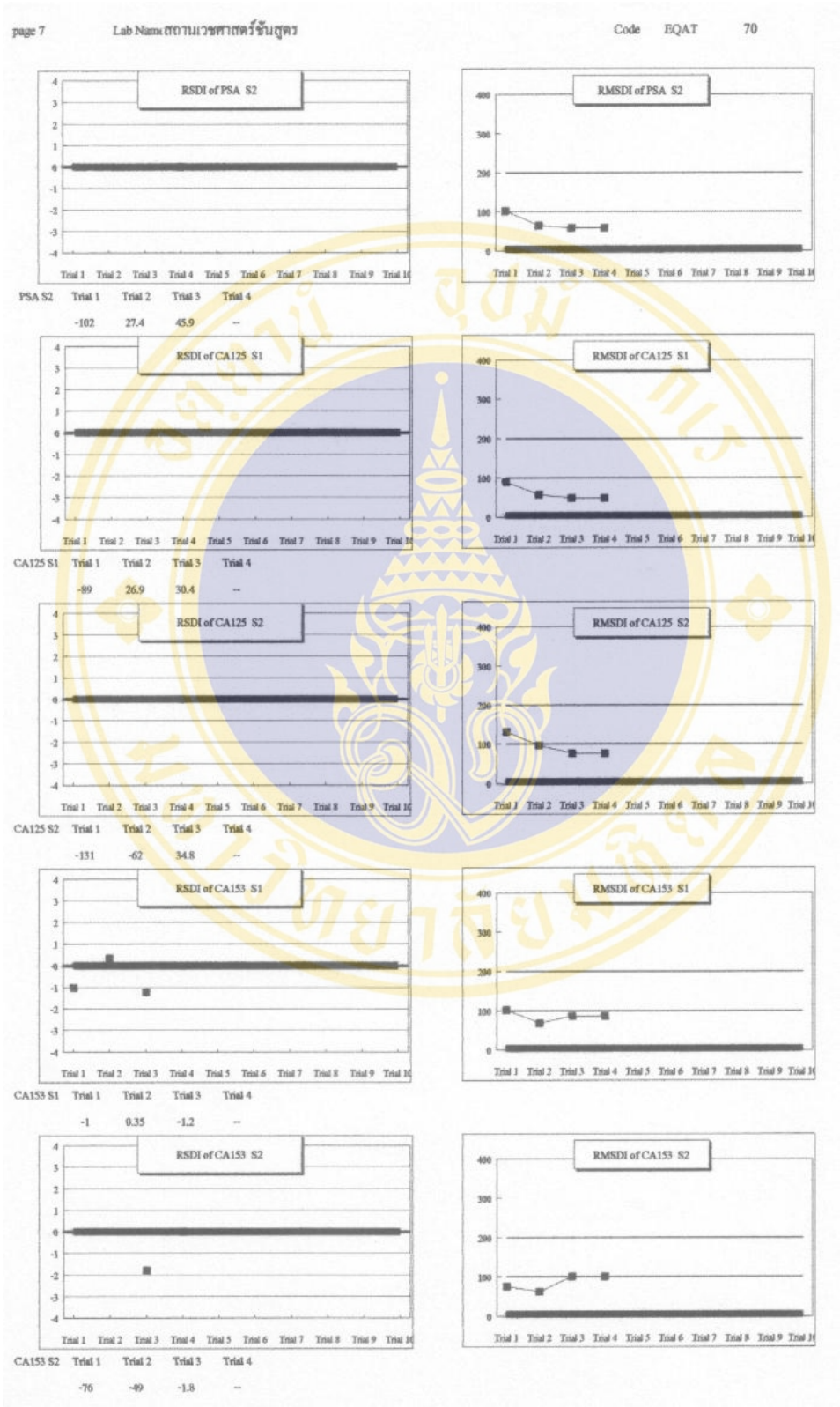

Figure 23G. Assessment report form page 7

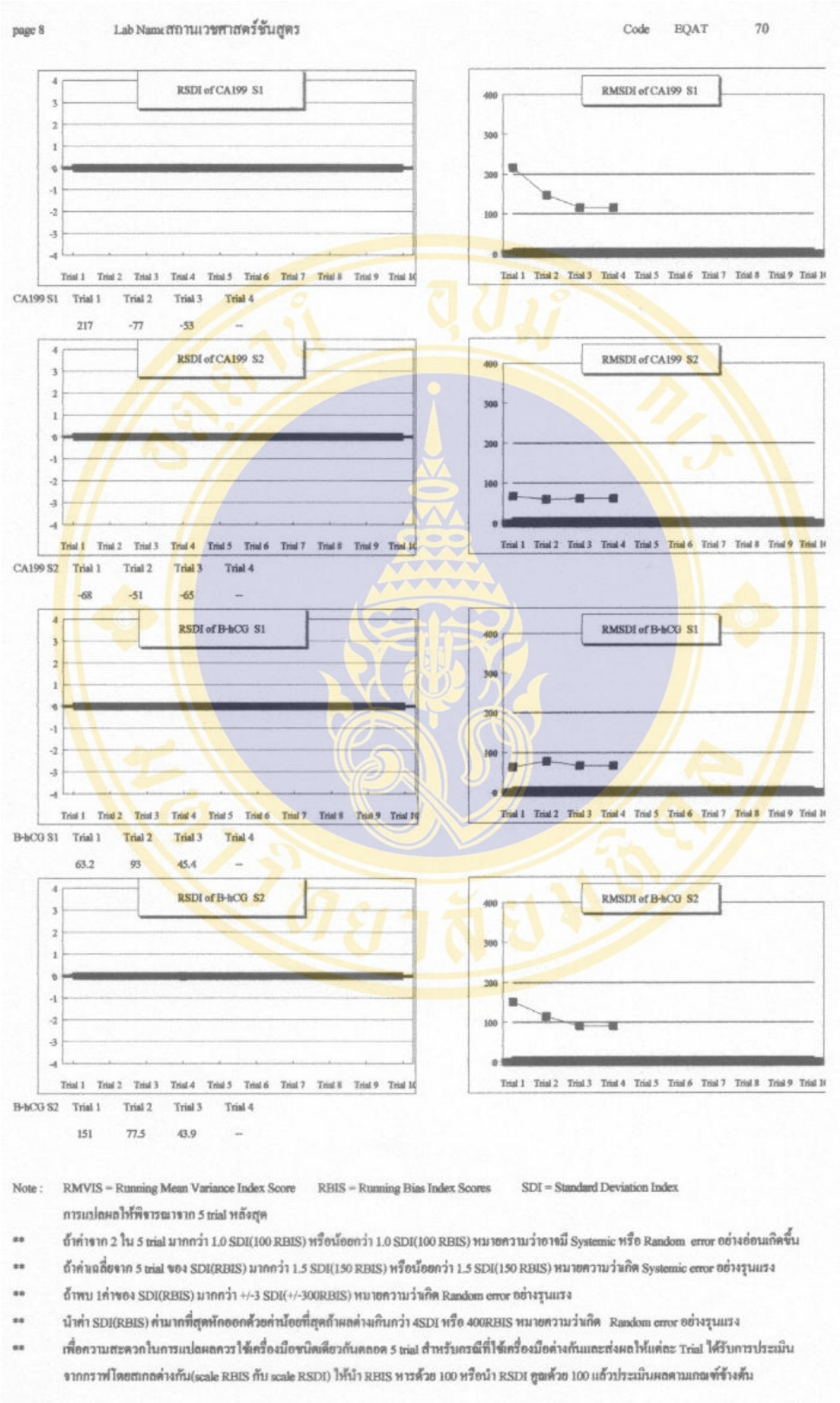

Figure 23H. Assessment report form page 8

Table 35. Designated values of sample control and number of participant (n) of AFP, CEA in the 1st, 2nd, 3rd, 4th, 5th, 6th trial

AFP (ng/ml)	S1 (n)	S2 (n)	S3 (n)	S4 (n)	S5 (n)	S6 (n)	S7 (n)	S8 (n)	S9 (n)	S10 (n)	S11 (n)	S12 (n)
Overall	64.6 (55)	560.8	55.7 (52)	17.4 (52)	54.0 (51)	18.6 (51)	1424.4	2181.4	63.5 (57)	19.6 (57)	14.6 (55)	2.2 (55)
AxSYM/IMX	65.6 (20)	580.8	60.3 (16)	14.7 (16)	55.4 (15)	17.9 (16)	1535.0	2367.9	64.2 (18)	19.5 (21)	14.4 (19)	2.2 (21)
Access	56.9 (6)	486.7 (6)	47.0 (5)	16.1 (6)	49.5 (6)	16.7 (6)	1411.9	1958.9	59.7 (5)	18.8 (5)	14.9 (4)	2.2 (4)
minividas	61.8 (4)	560.8 (4)	51.9 (1)	15.6 (1)	53.6 (2)	15.8 (2)	1665.5	2966.5	62.9 (2)	19.5 (2)	16.6 (2)	1.8 (2)
Immulite	52.0 (1)	537.0 (1)	53.0 (1)	15.4 (1)	55.9 (1)	17.6 (1)	1230.0	2260.0	59.4 (1)	18.2 (1)	16.2 (1)	1.7 (1)
Vitros Eci			55.6 (3)	17.0 (3)	48.1 (2)	16.4 (2)	1345.8	2014.3	59.3 (5)	18.4 (5)	14.2 (4)	1.9 (4)
Cobas core	59.1 (5)	583.2 (4)	69.2 (5)	17.8 (4)	61.1 (4)	18.5 (4)	1555.3	2248.2	67.1 (6)	18.7 (5)	13.7 (5)	2.0 (5)
Elecsys	65.4 (11)	525.7	54.3 (13)	16.3 (13)	52.4 (14)	17.6 (14)	1357.9	2328.1	61.4 (12)	18.5 (11)	14.2 (12)	2.1 (12)
Others	64.6 (2)		32.4 (2)	20.1 (2)	66.9 (1)	23.1 (1)	1589.0	1436.0	66.1 (2)	20.6 (2)	15.4 (2)	2.6 (2)
CEA (ng/ml)	**S1 (n)**	**S2 (n)**	**S3 (n)**	**S4 (n)**	**S5 (n)**	**S6 (n)**	**S7 (n)**	**S8 (n)**	**S9 (n)**	**S10 (n)**	**S11 (n)**	**S12 (n)**
Overall	11.1 (52)	8.3 (52)	10.7 (51)	1.9 (51)	16.9 (50)	2.5 (50)	28.6 (50)	164.4	10.4 (54)	1.9 (54)	1.8 (53)	2.0 (53)
AxSYM/IMX	10.6 (19)	7.8 (19)	9.9 (13)	1.9 (12)	16.5 (12)	2.1 (13)	27.1 (14)	160.4	9.6 (17)	1.8 (17)	1.8 (17)	2.0 (17)
Access	4.2 (6)	7.4 (5)	10.7 (6)	1.8 (6)	21.6 (5)	1.8 (4)	30.6 (4)	180.3 (4)	10.5 (4)	1.7 (4)	1.6 (4)	1.7 (4)
minividas	4.2 (4)	6.6 (5)	8.4 (3)	1.2 (3)	16.6 (3)	1.4 (3)	26.9 (3)	170.3 (3)	9.2 (4)	1.3 (4)	1.2 (4)	1.4 (4)
Immulite	14.2 (1)	10.0 (1)	13.6 (1)	1.9 (1)	24.1 (1)	2.2 (1)	36.0 (1)	212.0 (1)	12.2 (1)	1.7 (1)	2.1 (1)	2.2 (1)
Vitros Eci	23.9 (1)	8.9 (1)	11.3 (3)	1.6 (3)	7.6 (2)	9.2 (2)	32.9 (4)	189.1 (4)	11.7 (5)	1.6 (4)	1.6 (3)	1.8 (3)
Cobas core	12.4 (2)	9.5 (4)	13.6 (2)	2.2 (3)	20.3 (3)	2.6 (3)	30.9 (4)	191.2 (3)	12.6 (4)	2.2 (4)	2.2 (3)	2.6 (3)
Elecsys	15.4 (7)	9.0 (13)	10.3 (17)	2.1 (16)	16.7 (16)	2.5 (18)	26.5 (15)	145.7	10.3 (14)	2.0 (14)	2.0 (13)	2.1 (13)
Others	28.0 (1)	10.9 (1)	13.7 (2)	2.7 (2)	15.1 (2)	2.8 (2)	34.8 (2)	170.2 (1)	15.9 (2)	2.9 (2)	2.9 (2)	3.0 (2)

Table 36. Designated values of control sample and number of participant (n) of PSA, CA125 in the 1st, 2nd, 3rd, 4th, 5th, 6th trial

PSA (ng/ml)	S1 (n)	S2 (n)	S3 (n)	S4 (n)	S5 (n)	S6 (n)	S7 (n)	S8 (n)	S9 (n)	S10 (n)	S11 (n)	S12 (n)
Overall	6.6 (41)	0.3 (40)	0.4 (39)	0.4 (39)	1.0 (40)	0.4 (40)	0.4 (42)	0.3 (42)	0.4 (47)	0.4 (47)	11.8 (44)	19.1 (44)
AxSYM/IMX	7.8 (15)	0.3 (18)	0.3 (14)	0.3 (12)	1.0 (10)	0.4 (10)	0.4 (13)	0.2 (13)	0.4 (15)	0.4 (16)	14.7 (15)	24.2 (15)
Access	6.6 (5)	0.5 (5)	0.4 (4)	0.4 (4)	0.9 (5)	0.4 (5)	0.4 (3)	0.3 (4)	0.4 (3)	0.4 (3)	11.3 (2)	17.7 (2)
minividas	6.8 (4)	0.4 (4)	0.5 (4)	0.5 (4)	1.1 (4)	0.4 (4)	0.4 (5)	0.5 (5)	0.5 (5)	0.5 (4)	11.5 (5)	18.3 (5)
Immulite	6.8 (1)	0.3 (1)	0.5 (1)	0.4 (1)	1.0 (1)	0.3 (1)	0.3 (1)	0.2 (1)	0.3 (1)	0.3 (1)	15.0 (1)	24.5 (1)
Vitros Eci	4.5 (1)	0.5 (1)	0.6 (2)	0.6 (2)	1.2 (2)	0.6 (2)	0.4 (4)	0.4 (4)	0.6 (6)	0.6 (6)	8.4 (4)	13.5 (4)
Cobas core	4.5 (2)	0.2 (2)	0.3 (1)	0.3 (1)								
Elecsys	6.0 (7)	0.3 (7)	0.4 (9)	0.4 (10)	0.9 (9)	0.4 (11)	0.4 (8)	0.3 (9)	0.4 (10)	0.4 (10)	10.5 (10)	17.2 (11)
Others	6.2 (1)	0.2 (1)	0.4 (1)	0.4 (1)	0.8 (2)	0.4 (1)	0.4 (1)	0.3 (1)	1.1 (2)	1.2 (2)	9.6 (2)	16.0 (2)
CA125(U/ml)	**S1 (n)**	**S2 (n)**	**S3 (n)**	**S4 (n)**	**S5 (n)**	**S6 (n)**	**S7 (n)**	**S8 (n)**	**S9 (n)**	**S10 (n)**	**S11 (n)**	**S12 (n)**
Overall	12.5 (19)	24.3 (19)	23.5 (17)	13.1 (17)	14.7 (16)	11.6 (16)	145.5 (15)	132.3 (15)	18.4 (21)	12.1 (21)	11.7 (20)	11.3 (20)
AxSYM/IMX	10.9 (9)	23.6 (10)	18.0 (8)	12.4 (9)	12.4 (6)	9.7 (6)	144.2 (7)	132.4 (6)	16.5 (9)	10.7 (9)	11.1 (9)	11.0 (8)
Access												
minividas		15.0 (1)	14.2 (1)	9.0 (1)	10.9 (1)	8.6 (1)	135.9 (1)	121.8 (1)	13.7 (1)	9.6 (1)	7.8 (1)	7.7 (1)
Immulite												
Vitros Eci					15.0 (1)	12.0 (1)	150.5 (2)	136.0 (2)	17.2 (3)	11.0 (3)	9.0 (2)	8.7 (2)
Cobas core	14.5 (1)	30.0 (1)					147.2 (5)		24.3 (1)	16.3 (1)	16.3 (1)	15.8 (1)
Elecsys	14.0 (4)	25.1 (6)	22.2 (5)	15.7 (5)	17.6 (5)	14.6 (5)		129.0 (5)	21.2 (4)	16.2 (5)	13.7 (4)	13.8 (4)
Others	11.8 (1)	29.4 (1)	21.4 (1)	12.9 (1)	13.2 (1)	8.2 (1)			15.8 (1)	4.7 (1)	4.1 (1)	3.8 (1)

Table 37. Designated values of control sample and number of participant (n) of CA15-3, CA19-9 in the 1st, 2nd, 3rd, 4th, 5th, 6th trial

CA15-3 (U/ml)	S1 (n)	S2 (n)	S3 (n)	S4 (n)	S5 (n)	S6 (n)	S7 (n)	S8 (n)	S9 (n)	S10 (n)	S11 (n)	S12 (n)
Overall	11.2 (13)	13.0 (13)	23.5 (13)	10.6 (13)	17.7 (11)	10.9 (11)	40.1 (11)	26.6 (11)	22.8 (15)	11.4 (15)	11.0 (13)	11.7 (13)
AxSYM/IMX	10.3 (4)	12.3 (5)	16.9 (4)	9.3 (5)	16.7 (4)	9.8 (4)	36.5 (4)	23.5 (4)	17.9 (5)	9.5 (5)	9.2 (5)	10.0 (5)
Access				10.6 (1)								
minividas	11.0 (1)	13.0 (1)	21.2 (1)		17.2 (1)	11.8 (1)	40.8 (2)	28.9 (2)	22.3 (3)	12.0 (3)	11.1 (1)	11.2 (1)
Immulite												
Vitros Eci	8.0 (1)								28.0 (1)	13.4 (1)	13.6 (1)	14.4 (1)
Cobas core	12.0 (6)	11.0 (1)	23.4 (1)	10.4 (1)					25.3 (1)	15.6 (1)	14.5 (1)	16.4 (1)
Elecsys		13.4 (5)	27.6 (6)	11.8 (6)	18.0 (5)	11.6 (6)	42.7 (5)	28.1 (5)	26.4 (5)	11.7 (5)	11.4 (5)	12.1 (5)
Others												
CA19-9 (U/ml)	**S1 (n)**	**S2 (n)**	**S3 (n)**	**S4 (n)**	**S5 (n)**	**S6 (n)**	**S7 (n)**	**S8 (n)**	**S9 (n)**	**S10 (n)**	**S11 (n)**	**S12 (n)**
Overall	6.1 (17)	207.7 (17)	88.4 (16)	12.0 (16)	28.3 (14)	13.3 (14)	22.6 (11)	600.7 (11)	90.8 (15)	11.9 (15)	6.7 (15)	10.2 (15)
AxSYM/IMX	4.5 (8)	204.8 (7)	88.0 (7)	9.9 (7)	26.7 (7)	10.5 (6)	19.0 (4)	524.9 (3)	99.1 (6)	9.2 (6)	4.3 (7)	7.3 (6)
Access												
minividas	5.0 (1)	302.0 (1)	103.9 (1)	12.2 (1)	36.9 (1)	15.1 (1)	19.1 (1)	900.9 ((1)	101.5 (1)	12.4 (1)	6.2 (1)	8.4 (1)
Immulite												
Vitros Eci												
Cobas core	6.0 (2)	302.5 (2)	101.6 (1)	16.1 (1)					102.5 (1)	16.9 (1)	7.6 (1)	12.9 (1)
Elecsys	9.2 (5)	181.2 (5)	78.8 (6)	14.5 (5)	28.7 (6)	15.8 (5)	26.0 (4)	533.8 (5)	77.1 (5)	13.5 (5)	8.8 (5)	12.5 (5)
Others												

Table 38. Designated values of control sample and number of participant (n) of β-hCG in the 1st, 2nd, 3rd, 4th, 5th, 6th trial

β-hCG (mIU/ml)	S1 (n)	S2 (n)	S3 (n)	S4 (n)	S5 (n)	S6 (n)	S7 (n)	S8 (n)	S9 (n)	S10 (n)	S11 (n)	S12 (n)
Overall	45.3 (38)	8.1 (38)	59.1 (43)	61.3 (43)	92.1 (45)	93.6 (45)	33.0 (45)	44.8 (45)	60.0 (48)	60.0 (48)	19.8 (45)	469.6 (45)
AxSYM/IMX	49.2 (12)	6.9 (12)	57.9 (11)	58.9 (13)	99.1 (13)	99.1 (13)	32.5 (13)	45.9 (13)	62.0 (13)	62.9 (13)	20.0 (15)	536.9 (14)
Access	37.1 (3)	6.7 (3)	76.8 (2)	76.9 (2)	104.9 (2)	104.7 (2)	41.3 (2)	55.4 (2)	78.8 (2)	76.1 (2)	30.7 (1)	756.1 (1)
minividas	49.9 (4)		57.6 (4)	56.6 (4)	82.7 (4)	84.1 (4)	29.3 (4)	39.3 (4)	50.2 (4)	51.3 (4)	17.3 (3)	398.1 (3)
Immulite	57.0 (1)	12.0 (1)	47.3 (1)	47.4 (1)	89.4 (1)	81.5 (1)	28.4 (1)	38.9 (1)	47.5 (1)	47.5 (1)	20.1 (1)	411.0 (1)
Vitros Eci	57.0 (1)	12.0 (1)	60.1 (3)	59.9 (3)	87.6 (2)	85.9 (3)	33.6 (5)	44.7 (5)	58.1 (4)	57.6 (4)	19.6 (3)	423.0 (3)
Cobas core	42.7 (5)	5.0 (4)	72.8 (6)	72.4 (6)	98.8 (6)	100.3 (6)	38.0 (7)	50.7 (7)	67.7 (7)	68.3 (7)	20.1 (5)	485.2 (6)
Elecsys	40.0 (5)	7.1 (6)	56.4 (9)	55.7 (9)	85.4 (11)	83.5 (11)	31.7 (9)	42.5 (9)	54.6 (10)	55.0 (10)	19.2 (11)	413.8 (11)
Others	26.2 (2)	27.7 (2)	61.9 (1)	62.8 (1)	87.4 (1)	74.8 (1)	34.5 (1)	41.9 (1)	50.0 (2)	51.4 (2)	19.8 (2)	416.0 (2)

ที่ สธ 0319/11348

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14 กันยายน 2545

เรื่อง ผลการพิจารณาในการขอความอนุเคราะห์ให้นักศึกษาเก็บตัวอย่างชีรั่ม เพื่อประกอบการทำวิทยานิพนธ์

เรียน หัวหน้าภาควิชาเคมีคลินิก คณะเทคนิคการแพทย์ มหาวิทยาลัยมหิดล

ตามหนังสือที่ ทม 0804.02/166 ลงวันที่ 5 มิถุนายน 2545 เรื่องขอความอนุเคราะห์ให้ นายฉัตรชัย มังกรแสงแก้ว นักศึกษาปริญญาโท วิชาเทคนิคการแพทย์ คณะเทคนิคการแพทย์ มหาวิทยาลัยมหิดล ซึ่งอยู่ระหว่างการทำวิทยานิพนธ์เรื่อง "Organizing of National External Quality Assessment Schemes In Tumour Markers (A Pilot Project)" ซึ่งกำลังเตรียมตัวอย่างคอนโทรลทูเมอร์มาร์คเกอร์ และศึกษาความเหมาะสมในการนำมาใช้ในโครงการนำร่องซึ่งเป็นวิทยานิพนธ์ดังกล่าว เก็บตัวอย่างชีรั่มเพื่อการจัดเตรียมตัวอย่าง โดยขอรับคำปรึกษาจาก คุณศิริรัตน์ ตันสกุล เพื่อการจัดเก็บที่เหมาะสมด้วยนั้น

สถาบันมะเร็งแห่งชาติ ได้พิจารณาแล้วและอนุญาตให้ นายฉัตรชัย มังกรแสงแก้ว ดำเนินการเก็บตัวอย่างชีรั่มได้ โดยให้นักศึกษากำหนดจำนวนตัวอย่างชีรั่มที่แน่นอน และเมื่อนักศึกษาได้ทำวิทยานิพนธ์เสร็จเรียบร้อยแล้ว ขอให้จัดส่งวิทยานิพนธ์ให้แก่สถาบันมะเร็งแห่งชาติ จำนวน 1 เล่ม เพื่อสถาบันมะเร็งแห่งชาติจะเก็บไว้ สำหรับเป็นข้อมูลทางวิชาการต่อไป

จึงเรียนมาเพื่อโปรดทราบ และแจ้งผลการพิจารณานี้แก่ นายฉัตรชัย มังกรแสงแก้ว ต่อไปด้วย จะเป็นพระคุณ

ขอแสดงความนับถือ

พันตรี
(ชล กาญจนบัตร)
นายแพทย์ 9วช.
รักษาราชการแทน ผู้อำนวยการสถาบันมะเร็งแห่งชาติ

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Figure 24. Data collection permission

BIOGRAPHY

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