Ann. Ist. Super. Sanità, vol. 31, n. 1 (1995), pp. 21-35

Quality assurance programs in the United States

Noel S. LAWSON (*)

Department of Pathology, St. John Hospital and Medical Center and Wayne State University School of Medicine, Detroit, Michigan, USA

Summary. - The College of American Pathologists (CAP) provides quality assurance programs for clinical laboratories, including surveys for external quality assessment, quality assurance service for internal and regional quality control, and Q-probes for overall quality assurance including pre- and post-analytic factors. These are complemented by inspections through the laboratory accreditation program and a standards program linked with the national reference system for clinical chemistry. Expert resource committees, organized according to scientific disciplines, provide professional support and direction for these programs. Numerous other professional societies jointly sponsor various surveys, which optimize available expertise, size, and quality of these programs. CAP surveys are the most widely used programs for proficiency testing (PT) in the United States. PT programs only partially characterize performance. Clinical laboratories are best evaluated by a combination of measures, including EQA, internal and regional quality control, monitors of pre- and post-analytic quality, and inspection.

Key words: proficiency testing, quality control, regional quality control, quality assurance, standards, external quality assessment, laboratory accreditation.

Riassunto *(Programmi per la garanzia di qualità negli Stati Uniti)*. - Il College of American Pathologists (CAP) organizza programmi per la garanzia di qualità nei laboratori clinici che comprendono indagini di valutazione esterna di qualità, un servizio per la garanzia di qualità dedicato al controllo di qualità interno e regionale, infine test per la garanzia di qualità totale che riguardano fattori pre-analitici e post-analitici. A questi programmi di controllo si aggiungono le ispezioni nei laboratori, il programma per l'accreditamento e il programma per gli standard collegato con il sistema di riferimento nazionale per la chimica clinica. Comitati di esperti per le diverse discipline danno il supporto professionale e le direttive di questi programmi. Per ottenere un livello ottimale di professionalità, dimensioni e qualità dei programmi stessi viene richiesto congiuntamente il patrocinio di numerose altre società professionali. Le indagini di sorveglianza del CAP sono i programmi di "proficiency testing" più diffusi negli Stati Uniti. Tali programmi, tuttavia, caratterizzano solo parzialmente le prestazioni dei laboratori; per una valutazione ottimale sono necessari un insieme di interventi combinati: la valutazione esterna di qualità, il controllo di qualità interno e regionale, i test di qualità delle fasi pre-analitica e post-analitica, le ispezioni.

Parole chiave: controllo di qualità, controllo di qualità regionale, garanzia di qualità, standard, valutazione esterna di qualità, accreditamento dei laboratori.

Introduction

There are approximately 14,500 licensed hospital and independent clinical laboratories in the United States. Clinical laboratory quality assurance programs are sponsored, organized, and managed on state, regional, and national levels both by government and professional organizations. The College of American Pathologists (CAP) is a volunteer professional organization of approximately 14,700 physician specialists certified by the American Board of Pathology, and is the dominant provider of clinical laboratory quality assurance programs in the United States. This presentation focuses on professional programs for clinical laboratory quality assurance which are provided by CAP. The discussion emphasizes surveys for external quality assessment (EQA) or proficiency testing (PT), and quality assurance service (QAS) for internal and regional quality control.

The presentation includes information concerning laboratory professionals and their organizations, city, state, and federal government, the clinical laboratory manufacturing and supply industry, and participating laboratories. Program management and structure, interorganizational relationships, and governmental issues are emphasized over specific data obtained through these programs, which are extensive in breadth and quantity, and widely published in the medical literature. Interactions between internal and external quality control will be discussed, as will significant problems which we face in managing clinical laboratory quality assurance programs in the United States.

(*) Chairman, Quality Assurance Service-Quality Control (QAS-QC) Committee Member, Surveys Committee College of American Pathologists

External quality assessment in the United States

The initial EQA effort in the United States was a survey for syphilis serology that was initiated by the Centers for Disease Control (CDC) in the mid 1930's. The pioneering work of Belk and Sunderman, reported in 1947, used EQA to quantitate laboratory performance for hemoglobin, glucose, total protein, albumin, calcium, urea, and sodium chloride [1]. CAP initiated its EQA project in 1948, and developed a sustained and significant survey program in the early 1960's. The CAP surveys both assisted participating laboratories and described the state of laboratory practice as a public health measure.

The CAP surveys program for EQA has grown in numbers of disciplines, analytes, and participants. Presently, it serves approximately 13,000 traditional clinical laboratories as well as some 18,000 physician office laboratories. There are challenges on over 400 analytes in some 20 specialty areas. CAP surveys is the dominant EQA program in the United States. The program serves a large group of international subscribers, as well. Examples of surveys offered in chemistry, therapeutic drug analysis/endocrinology, and hematology are indicated in Tables 1-3. Increasingly, government has relied on EQA as a tool for proficiency testing (PT) and laboratory licensure [2].

Table 1. - Listing of CAP chemistry surveys available. The comprehensive survey includes commonly measured analytes in other listed surveys

Comprehensive	Trace metals
Electrophoresis/ chromatography	Cerebrospinal fluid
Linearity	Urine - basic
Linearity - lipid/enzyme	Urine - comprehensive
Linearity - therapeutic drugs	Critical care
Linearity - toxicology	Blood gas
Linearity - urine chemistry	Glycohemoglobin
Linearity - immunology	Lung maturity
Linearity - reproductive endocrinology	Neonatal bilirubin
Enzyme chemistry	Blood oximetry
isoenzymes	Whole blood glucose
	Pseudocholinesterase

Table 2. - Listing of CAP surveys in therapeutic drug testing and endocrinology. Basic surveys include commonly measured analytes

Therapeutic drug - basic
Therapeutic drug - comprehensive
Therapeutic drug - cyclosporine
Endocrinology (ligand) - basic
Endocrinology (ligand) - comprehensive
Maternal alpha-fetoprotein
Hormone receptors

Table 3. - Listing of CAP surveys in haematology. Because of requirements for specified control materials, there are seven separate surveys for automated flow-through differentials

Comprehensive
Comprehensive with flow-through differentials
Sysmex E series, M2000, K800, K1000, CC800, F-1
Coulter, Roche, Helios, Minos (Multiple)
Abbott Cell-Dyn 3000, 3500
Miles Technicon H1, H1 Jr., H2, H3
Abbott Cell-Dyn 610, 1400, 1500, 1600, 2000
Coulter STKS, VCS, MAXM
Sysmex NE 5500, 8000, 1500
Limited coagulation
Activated clotting time
Comprehensive coagulation
Hemoglobinometry

To manage the surveys program, CAP must provide both operational support and expert professional guidance. The CAP survey committee with designated management staff of the organization has the responsibility to contract for control materials, provide data processing support, solicit and obtain subscribers, produce participant and group reports, and validate laboratory performance to specified government agencies. Expert resource committees (Table 4) organized according to professional laboratory and scientific disciplines determine analytes to be surveyed, configuration and concentration of specific challenges, selected grading criteria, and structure of data output. In addition, these groups provide professional evaluations and critiques.

Other laboratory professional organizations participate through assigned liaison members serving on expert resource committees. Such organizations also jointly manage various surveys through co-sponsorship, e.g., The American Association for Clinical Chemistry, American Association of Blood Banks, American Society of Human Genetics, Foundation for Blood Research, and The American Society for Histocompatibility and Immunogenetics. Table 5 lists surveys co-sponsored with the American Association for Clinical Chemistry, and Table 6 lists joint programs with the American Association of Blood Banks.

The CAP surveys are accepted for PT purposes by virtually all responsible government regulatory units. Specific jurisdictions, however, may include a requirement for additional EQA. For example, the State of New York requires that licensed laboratories participate in its own program.

In addition to CAP, other professional organizations sponsor PT. The American Association of Bioanalysts (AAB) survey predominantly addresses small clients, including large numbers of independent laboratories. In terms of numbers of analytes, testing disciplines, size of

Table 4. - Expert/resource committees providing professional guidance to surveys in specified disciplines

AIDS and other bloodborne diseases
Biochemical and molecular genetics
Chemistry
Coagulation
Cytogenetics
Diagnostic immunology
Forensic pathology
Hematology/Clinical microscopy
Histocompatibility
Imaging (radioisotopic)
Instrumentation
Microbiology
Parentage testing
Reproductive biology
Therapeutic drug monitoring/ endocrinology
Toxicology
Transfusion medicine
Transfusion transmitted viruses

Table 5. - Listing of CAP chemistry related surveys with joint sponsorship of American Association for Clinical Chemistry

Whole blood cyclosporine
Whole blood alcohol/volatiles
Serum alcohol/volatiles
Blood lead
Forensic urine drug testing screening/confirmatory
Athletic drug testing

subscriber group, and complexity of output, the AAB Program is less comprehensive than that of CAP. The American Association for Clinical Chemistry had provided surveys in endocrinology and therapeutic drug measurement which are now consolidated with those of CAP. The California Thoracic Society operates an external quality assessment program for blood gas analysis. As a general rule, interorganizational cooperation yielding limited numbers of large integrated programs is preferable to multiple small schemes, as larger EQA programs benefit from sharing of expertise, reduced cost per unit of service, and maximized participant population to facilitate the collection of statistically valid data.

Evaluation criteria

Multiple strategies have evolved which address evaluation of participants' survey performance. These comprise two categories, i.e., selecting the target or putative correct value, and determining the limits of acceptable performance.

Since CAP surveys are peer comparison programs, target values have been significantly based on method-specific participant data. For those analytes generating continuous variable data, e.g., commonly measured chemistry and hematology analytes, target values are derived from participant data, following outlier exclusion. Gaussian statistics are employed, unless alternate distributions warrant other approaches. Means derived from all methods or other reliable comparative methods may also be used. Surveys may use weighed-in target values for nonindigenous analytes such as therapeutic drugs. When method groups contain small numbers of participants, target values are not obtained from method-specific peer data, but are derived from similar methods, all methods, or another designated comparative method. Analytes requiring identification of unknowns, e.g., microbiology cultures, parasite identification, and cytogenetic phenotype, use consensus by highly accurate laboratories to establish a correct result.

Given resource committees vary their evaluation strategies according to discipline and analyte, but always attempt to select the most reliable values. CAP periodically validates participant-based data against results by definitive methods as measured at the National Bureau of Standards, NBS (now renamed the National Institute of Standards and Technology, NIST), [3, 4]. Analytes that have been studied in this manner include calcium, chloride, cholesterol, creatinine, glucose, potassium, sodium, urea, and uric acid. For these analytes, the comparative method means are used as definitive method correlated target values, as opposed to peer group means used elsewhere. Table 7 lists general chemistry analytes with selection criteria for comparative methods.

Evaluation limits of acceptable results are either fixed, derived from participant data following application of statistical parameters, or a combination thereof. Fixed limits may be chosen when testing meeting these criteria indicates medically acceptable performance. Fixed limits are commonly applied to analytes measured with low error, where usual statistically based grading, e.g., classifying the central 95% as acceptable, would exclude laboratories who are performing satisfactorily for medical purposes. Examples of regulated evaluation criteria for

Table 6. - Listing of CAP surveys with joint sponsorship of American Association of Blood Banks

Viral markers
Donor module
Diagnostic module
Western blot/supplemental assays
Parentage testing
Forensic identity

Table 7. - Comparative methods used for statistical purposes to achieve grading with method groups of n < 10 or when an unlisted or unspecified method is given. For analytes with no comparative method, method groups of n < 10 are not evaluated. For analytes (*), all methods are graded against this definitive method correlated target value

Comparative methods	General chemistry surveys
ALT/SGPT	No comparative method
Albumin	Dye binding, BCG, rapid absorbance, all instruments
Alkaline phosphatase	No comparative method
Amylase	No comparative method
AST/SGOT	No comparative method
Bilirubin, total	All methods
* Calcium	All methods
* Chloride	Common groups, all automated instruments
* Cholesterol	Enzymatic, all multiconstituent analyzers
CK-MB	No comparative method
Cortisol	All methods
Creatine kinase (CK)	No comparative method
* Creatinine	All methods
* Glucose	Glucose oxidase O_2 electrode, all instruments
hCG	No comparative method
HDL cholesterol	No comparative method
Iron	All methods
Lactate dehydrogenase (LD)	No comparative method
Lactic acid	No comparative method
Lipase	No comparative method
Lithium	All methods
Magnesium	All methods
Osmolality	Combined results, freezing point instruments
Phosphorus	All methods
* Potassium	All common groups, all instruments
Protein, total	Biuret, all instruments
* Sodium	All common groups, all instruments
T3 uptake	No comparative method
TSH	All methods
Thyroxine	All methods
Triglycerides	No comparative method
* Urea nitrogen	Urease with GLDH, all instruments
* Uric acid	Uricase, all instruments

various disciplines are given in Tables 8-12. With surveys measuring discrete variables such as bacteriology culture and blood type, limits of acceptability are established by the expert resource committees according to clinical and technical factors.

Surveys output

The work products of surveys are participant reports and performance evaluations (Fig. 1), and group summaries (Fig. 2). The specific laboratory reports (Fig. 1) include information on methods, instruments, target values, explanation of limits, standard deviation interval (SDI, or z-score), and an indication of acceptable or unacceptable performance. The SDI indicates the submitted result's relative distance from the target value in standard deviations. For the great majority of evaluations, results with SDI between -2.0 and +2.0 had been considered acceptable, prior to implementation of regulatory guidelines, and are still employed for selected nonregulated analytes, in combination with fixed limits.

In Fig. 2, data recapitulate the group results for inorganic phosphorus, from a survey mailed during the first quarter of 1994. Specific variables in the tabular data include mean, standard deviation (SD) and coefficient of variation (CV) by method categories and for all-methods.

Government interaction

Understanding the interrelation between government and the professional laboratory community is pivotal in studying quality assurance programs in the United States [5]. Licensure of and payment to laboratories is accompanied by a requirement to participate in PT. Because of inconsistent laws and regulations between and within jurisdictions, the Federal Government, in 1990, amended the 1967 clinical laboratory improvement act (CLIA '67) to require uniform PT, to be applied to future programs [6]. These requirements address both participating laboratories and sponsoring organizations.

College of American Pathologists

SURVEY SET: FH6 - A
CAP NUMBER: 17266-01-03-01 KIT# 01
ATTENTION: LABORATORY SUPERVISOR
INSTITUTION: ST JOHN HOSP & MEDICAL CENTER

1994

COMP.HEMATOLOGY - FH6

EVALUATION

PAGE 02

KIT MAILED: 02/15/94
QUEST. EVAL: 05/05/94

COPIES SENT TO: MICHIGAN

CONSTITUENT / UNIT OF MEASURE / YOUR REPORTED METHOD / COMPARATIVE METHOD	SPECIMEN	YOUR RESULT	EVAL CODE	MEAN	SD	NUMBER OF LABS	SDI	LIMITS OF ACCEPTABILITY LOWER	LIMITS OF ACCEPTABILITY UPPER
WHITE BLOOD CELL COUNT / THOUSAND/UL / COULTER STKS	FH6-01	3.3	13	3.44	.12	1400	-1.2	2.9	4.0
	FH6-02	8.1	13	8.54	.20	1396	-2.2	7.2	9.9
	FH6-03	12.3	13	12.89	.30	1405	-2.0	10.9	14.9
	FH6-04	12.4	13	12.78	.28	1404	-1.4	10.8	14.7
	FH6-05	25.7	13	26.21	.58	1398	-0.9	22.2	30.2
NO COMPARATIVE METHOD									
RED CELL COUNT (FH) / MILLION/UL / COULTER STKS	FH6-01	6.11	13	6.169	.084	1401	-0.7	5.79	6.54
	FH6-02	5.46	13	5.531	.072	1397	-1.0	5.19	5.87
	FH6-03	3.71	13	3.702	.050	1399	+0.2	3.48	3.93
	FH6-04	2.68	13	2.674	.038	1394	+0.2	2.51	2.84
	FH6-05	2.11	13	2.126	.031	1383	-0.5	1.99	2.26
NO COMPARATIVE METHOD									
HEMOGLOBIN / G/DL / COULTER STKS	FH6-01	17.4	13	17.83	.22	1400	-2.0	16.5	19.1
	FH6-02	12.4	13	12.62	.15	1390	-1.5	11.7	13.5
	FH6-03	10.6	13	10.90	.14	1400	-2.1	10.1	11.7
	FH6-04	7.9	13	8.05	.12	1404	-1.3	7.4	8.7
	FH6-05	6.5	13	6.59	.12	1389	-0.8	6.1	7.1
ALL INSTRUMENTS	FH6-01			17.88	.25	2421	-1.9		
	FH6-02			12.64	.16	2430	-1.5		
	FH6-03			10.90	.14	2437	-2.1		
	FH6-04			8.06	.13	2428	-1.2		
	FH6-05			6.61	.14	2435	-0.8		
HEMATOCRIT / PERCENT / COULTER STKS	FH6-01	50.9	13	51.29	.77	1401	-0.5	48.2	54.4
	FH6-02	36.4	13	36.76	.57	1400	-0.6	34.5	39.0
	FH6-03	31.5	13	31.45	.85	1403	+0.1	29.5	33.4
	FH6-04	22.4	13	22.39	.38	1402	+0.0	21.0	23.8
	FH6-05	18.0	13	18.20	.33	1398	-0.6	17.1	19.3
NO COMPARATIVE METHOD									

PLOTS OF THE RELATIVE DISTANCE OF YOUR RESULTS FROM TARGETS AS PERCENTAGES OF ALLOWED DEVIATION

-100=LOWER LIMIT 0=TARGET 100=UPPER LIMIT

TEST EVENT	-100 -50 0 50 100
FH6-94A	1211
FH6-93C	211-1
FH6-93B	1211
FH6-93A	112--1
FH6-94A	12--2
FH6-93C	1-31
FH6-93B	131
FH6-93A	13-1
FH6-94A	113
FH6-93C	13-1
FH6-93B	221
FH6-93A	122
FH6-94A	12-2
FH6-93C	122
FH6-93B	1112
FH6-93A	1-31

Fig. 1. - Example of laboratory's survey evaluation for hematology for five challenges (FH 01-05) in 1994. All results are acceptable. Report gives method, instrument, result, group mean, SDI, and number of laboratories in peer group. The scale of -100 to + 100 represents the relative scoring limits in percent on either side of the target value. Coicident points are indicated by values other than 1. The graphic output recapitulates the current specimens along with those of the three previous mailings.

SURVEY GROUP SUMMARY DATA

	------SPECIMEN C-01------				------SPECIMEN C-02------			
	NO. LABS	MEAN	S.D.	C.V.	NO. LABS	MEAN	S.D.	C.V.
PHOSPHORUS - MG/DL								
ALL METHOD PRINCIPLES								
**ALL INSTRUMENTS	5106	3.79	0.24	6.4	5077	7.79	0.31	4.0
PHOSPHOMOL. W/ANY RED.								
ABBOTT SPECTRUM	38	3.72	0.13	3.6	38	7.42	0.23	3.1
BECKMAN SY CX7/4CE/5CE	61	3.83	0.19	5.0	59	8.09	0.27	3.3
BECKMAN SYNCHRON CX4/5	23	3.75	0.13	3.4	23	7.99	0.27	3.4
CORNING 550 EXPRESS	17	3.85	0.26	6.8	17	7.53	0.49	6.6
KODAK EKTACHEM DT/DTII	13	3.61	0.13	3.7	13	7.44	0.28	3.7
KODAK EKTACHEM 250	66	4.06	0.08	2.0	64	7.75	0.14	1.8
KODAK EKTACHEM 400,700	945	4.05	0.09	2.2	936	7.75	0.16	2.0
KODAK EKTACHEM 500 ETC	256	4.03	0.11	2.8	253	7.72	0.17	2.3
ROCHE COBAS FARA/MIRA	33	3.35	0.16	4.7	34	7.54	0.29	3.9
TECH RA500,1000,XT2000	17	3.79	0.34	8.8	17	7.96	0.46	5.8
ALL AUTO CHEM INSTR	1464	4.01	0.14	3.4	1492	7.75	0.21	2.7
ALL MANUAL CHEM INSTR	13	3.61	0.13	3.7	13	7.44	0.28	3.7
PHOSPHOMOLYBDATE UV								
ABBOTT SPECTRUM	245	3.77	0.14	3.8	251	7.45	0.27	3.6
ABBOTT SPECTRUM EPX	48	3.77	0.13	3.5	46	7.33	0.23	3.1
BAXTER PARAMAX	524	3.58	0.09	2.4	524	7.68	0.19	2.5
BECKMAN SY CX7/4CE/5CE	383	3.79	0.16	4.2	385	8.08	0.26	3.3
BECKMAN SYNCHRON CX4/5	227	3.74	0.15	4.1	227	8.06	0.26	3.2
BM/H 704	63	3.61	0.20	5.5	63	7.74	0.30	3.9
BM/H 705	10	3.87	0.43	11.2	10	8.01	0.52	6.5
BM/H 717	278	3.66	0.14	3.8	278	7.84	0.28	3.5
BM/H 736	56	3.73	0.17	4.5	56	7.84	0.26	3.3
BM/H 737	44	3.65	0.18	5.0	43	7.85	0.30	3.8
BM/H 747	143	3.61	0.15	4.2	145	7.76	0.26	3.4
BM/H 911	112	3.58	0.15	4.2	110	7.74	0.28	3.6
CORNING 550 EXPRESS	56	3.88	0.24	6.2	56	7.61	0.41	5.4
COULTER DACOS	25	3.35	0.08	2.3	26	7.55	0.19	2.6
DUPONT ACA	61	3.79	0.21	5.5	60	7.91	0.31	3.9
DUPONT DIMENSION	595	3.83	0.11	2.8	596	7.95	0.21	2.6
IL MONARCH	138	3.81	0.22	5.9	136	7.65	0.39	5.0
OLYMPUS AU 5000	35	3.72	0.18	4.9	35	7.77	0.28	3.6
OLYMPUS DEMAND	11	3.77	0.36	9.4	11	7.73	0.43	5.6
OLYMPUS REPLY	32	3.48	0.17	4.8	33	7.58	0.36	4.7
ROCHE COBAS FARA/MIRA	212	3.39	0.21	6.2	214	7.51	0.35	4.6
TECH RA500,1000,XT2000	68	3.84	0.24	6.2	67	7.98	0.26	3.3
TECHNICON AXON	15	3.67	0.11	3.0	15	8.18	0.31	3.8
TECHNICON CHEM 1	43	3.66	0.15	4.1	43	7.91	0.28	3.5
TECHNICON DAX	31	3.61	0.10	2.8	31	8.02	0.19	2.3
ALL AUTO CHEM INSTR	3554	3.70	0.21	5.6	3548	7.81	0.34	4.4

Fig. 2. - Table with method specific data for two of five serum inorganic phosphorus challenges (C-01, C-02) in 1994. Data given for methods with 10 or greater users, and includes numbers of laboratories, mean values, SD, and CV according to methods, method categories, and for the tested population.

The requirements for uniform PT designate the laboratory sections to be regulated, selection of analytes which must be tested, frequency of testing, and grading criteria including strategies for selecting target values and limits of acceptable performance. The number of challenge specimens has been specified, with the majority of regulated analytes requiring a minimum of 20 (subsequently modified to 15) unknown samples per year. CAP's implementation of mandated changes commenced as of the 1991 survey year.

PT is also included in the clinical laboratory improvement amendments of 1988 (CLIA '88) legislation, whose final regulations were published in 1992 [7]. CLIA '88 includes personnel standards, classification of laboratories by testing complexity, and requirement for licensure of virtually all clinical laboratory testing sites, including freestanding screening entities and physician offices. As a result of the CLIA '67 uniform PT requirements and the CLIA '88 legislation, modified criteria for acceptable results are imposed. These are given in Tables 8-12. For most tests, three mailings per year are required, each with five challenges. A score of 80 percent or better is required for each analyte, and passing grades are required, accordingly, for two of three mailings. Unsuccessful participation in PT subjects a laboratory to sanctions, which in the extreme can preclude a laboratory from testing a specified analyte or group of analytes.

The dominant client base for CAP surveys is the traditional population of licensed clinical laboratories. CAP cooperates with the American Society of Internal Medicine, American Academy of Family Physicians, American Academy of Pediatrics, and American Osteopathic Association, to provide voluntary proficiency testing programs for physicians' office laboratories (POL). With the definitive implementation of Federal regulations requiring POLs to undergo proficiency testing, some 37,000 of these laboratories have registered, and participate in PT. EQA programs for physicians' offices are less complex than traditional programs. Most commonly they challenge a relatively small group of common analytes in hematology, basic chemistry, urinalysis, and immunology.

Internal and regional quality control

EQA is only partially effective in characterizing laboratory performance. Indeed, the real-time daily routine operation of a laboratory, as quantitated through internal quality control, is a truer indicator. Whereas EQA programs traditionally utilize unknown samples received from outside the laboratory, internal quality control, through the control sample technique, employs specimens whose concentrations are known. These

Table 8. - Clinical laboratory improvement amendments of 1988 (CLIA '88), regulated evaluation limits for immunology analytes

Analyte or test	Criteria for acceptable performance
Alpha-1 antitrypsin	Target value ± 3 SD
Alpha-fetoprotein (tumor marker)	Target value ± 3 SD
Antinuclear antibody	Target value ± 2 dilutions or positive or negative
Antistreptolysin O	Target value ± 2 dilutions or positive or negative
Anti-human immunodeficiency virus	Reactive or nonreactive
Complement C3	Target value ± 3 SD
Complement C4	Target value ± 3 SD
Hepatitis (HBsAg, anti-HBc, HBeAg)	Reactive (positive) or nonreactive (negative)
IgA	Target value ± 3 SD
IgE	Target value ± 3 SD
IgG	Target value ± 25%
IgM	Target value ± 3 SD
Infectious mononucleosis	Target value ± 2 dilutions or positive or negative
Rheumatoid factor	Target value ± 2 dilutions or positve of negative
Rubella	Target value ± 2 dilutions or immune or nonimmune or positive or negative

routines focus on ascertaining the appropriateness of releasing patient data in real time, through the application of statistically based quality control rules. When extended to regional quality control, they allow assessment of bias and precision relative to peers. To address internal and extended internal or regional quality control, CAP has established the quality assurance service (QAS) program, managed by the quality assurance service-quality control (QAS-QC) committee and designated staff.

QAS operates in cooperation with large groups of laboratories, usually in cohesive geographic regions, who share pools of control materials for their daily use. Programs are typically sponsored, organized, and managed by one or more state pathology societies. Programs contract with vendors to provide large uniform stable lots of control materials. With the CAP QAS program, data processing, management coordination, and interlaboratory comparative statistics are provided [8, 9]. Presently, there are approximately 1,600 laboratories in the United States and Canada enrolled in the QAS program in chemistry, endocrinology, therapeutic drug analysis, hematology, and coagulation. Various commercial controls are employed, such as lyophilized serum, stabilized liquid serum, lyophilized plasma, and whole blood simulators. Because these controls are used on a daily basis, pools of large volume are required. Limitations in manufacturing capacity restrict maximum lot size and therefore the number of participants who are able to analyze a single pool simultaneously. Regional quality control programs for clinical chemistry each have approximately 100-400 participants sharing controls for some 12-18 months.

Table 9. - Clinical laboratory improvement amendments of 1988 (CLIA '88), regulated evaluation limits for clinical chemistry analytes

Analyte or test	Criteria for acceptable performance
Alanine aminotransferase (ALT/SGPT)	Target value ± 20%
Albumin	Target value ± 10%
Alkaline phosphatase	Target value ± 30%
Amylase	Target value ± 30%
Aspartate aminotransferase (AST/SGOT)	Target value ± 20%
Bilirubin, total	Target value ± 0.4 mg/dl or ± 20% (greater)
Blood gas pO2	Target value ± 3 SD
pCO2	Target value ± 5 mm Hg or ± 8% (greater)
pH	Target value ± 0.04
Calcium, total	Target value ± 1.0 mg/dl
Chloride	Target value ± 5%
Cholesterol, total	Target value ± 10%
Cholesterol, high density lipoprotein	Target value ± 30%
Creatine kinase	Target value ± 30%
Creatine kinase isoenzymes	MB elevated (presence or absence) or target value ± 3 SD
Creatinine	Target value ± 0.3 mg/dl or ± 15% (greater)
Glucose (excluding glucose performed on monitoring devices cleared by United States Food and Drug Administration, FDA, for home use)	Target value ± 6 mg/dl or ± 10% (greater)
Iron, total	Target value ± 20%
Lactate dehydrogenase (LDH)	Target value ± 20%
LDH isoenzymes	LDH1/LDH2(+ or -) or target value ± 30%
Magnesium	Target value ± 25%
Potassium	Target value ± 0.5mmol/l
Sodium	Target value ± 4 mmol/l
Total protein	Target value ± 10%
Triglycerides	Target value ± 25%
Urea nitrogen	Target value ± 2 mg/dl or ± 9% (greater)
Uric acid	Target value ± 17%

Certain manufacturers provide client laboratories with an interlaboratory data program as an adjunct to their internal quality control materials. The aggregate number of participants in the various commercial programs exceeds that of the CAP sponsored program. The CAP QAS program provides professional data review, multiple levels of outlier exclusion criteria, uniform method taxonomy coordinated with that used in CAP surveys, and scientific input of CAP resource committees. The degree of such value-added services in industry-based programs is limited.

QAS surveys accuracy based control (shared pools/CrossLink) program

CAP has developed a combined surveys-QAS shared pools (CrossLink) program in which designated manufactured lots are distributed initially as survey challenges, and subsequently made available to participants in regional quality control programs. This program facilitates upgrading of traditional internal quality control to accuracy based control. Surveys for EQA provide statistically reliable target values, leading to highly valid assessments of analytic bias. Due to the relatively small numbers of challenges, only limited information is available from EQA for estimates of precision. Daily internal quality control within regional programs offers highly reliable data for analytic precision. The quality of data for bias is less assured, due to the limitation in numbers of participants engendered by maximum pool size. The shared pool program provides target value assessment with the reliability of surveys, and precision estimates from daily quality control data. Therefore, the composite data on bias, precision, and total error, for individual laboratories and the participant group, are considered to be highly reliable. The shared pool program, furthermore, provides renewable target values within the monthly group data reduction. This updates target values originally assigned in this program

Table 10. - Clinical laboratory improvement amendments of 1988 (CLIA '88), regulated evaluation limits for endocrinology analytes

Analyte or test	Criteria for acceptable performance
Cortisol	Target value ± 25%
Free thyroxine	Target value ± 3 SD
Human chorionic gonadotropin	Target value ± 3 SD positive or negative
T3 uptake	Target value ± 3 SD
Triiodothyronine	Target value ± 3 SD
	Target value ± 3 SD
Thyroid-stimulating hormone	Target value ± 20% or 1.0
Thyroxine	mcg/dl (greater)

Table 11. - Clinical laboratory improvement amendments of 1988 (CLIA '88), regulated evaluation limits for toxicology analytes

Analyte or test	Criteria for acceptable performance
Alcohol, blood	Target value ± 25%
Blood lead	Target value ± 10% or 4 mcg/dl (greater)
Carbamazapine	Target value ± 25%
Digoxin	Target value ± 20% or ± 0.2 ng/ml (greater)
Ethosuximide	Target value ± 20%
Gentamicin	Target value ± 25%
Lithium	Target value ± 0.3 mmol/l or ± 20% (greater)
Phenobarbital	Target value ± 20%
Phenytoin	Target value ± 25%
Primidone	Target value ± 25%
Procainamide (and metabolite)	Target value ± 25%
Quinidine	Target value ± 25%
Tobramycin	Target value ± 25%
Theophylline	Target value ± 25%
Valproic acid	Target value ± 25%

Table 12. - Clinical laboratory improvement amendments of 1988 (CLIA '88), regulated evaluation limits for haematology analytes

Analyte or test	Criteria for acceptable performance
Cell identification	90% or greater consensus on identification
White blood cell differential	Target ± 3 SD based on the percentage of different types of white blood cells in the samples
Erythrocyte count	Target ± 6%
Hematocrit (excluding spun hematocrits)	Target ± 6%
Hemoglobin	Target ± 7%
Leukocyte count	Target ± 15%
Platelet count	Target ± 25%
Fibrinogen	Target ± 20%
Partial thromboplastin time	Target ± 15%
Prothrombin time	Target ± 15%

(as would also pertain to commercial assayed serum) wherein reagent or calibrator shifts occurring during the life of the control lot cause changes in targets on matrix controls [10].

QAS output

QAS provides reports with data both specific by participant and summarized for the testing population. Fig. 3 indicates the statistical output for an individual laboratory, with results from selected common analytes. Fig. 4 provides a tabulated group summary with data on inorganic phosphorus.

Reports include the intralaboratory values for mean, SD, and CV, supplemented by key interlaboratory comparative data on bias (SDI) and relative precision. A three-tiered comparison, sorted by specific method (e.g., instrument-method principle combination), general method (method principle), and all manual/semiautomated or automated methods is included. Because multiple pools with different analyte concentrations are used, the data is lot-specific, grouped around individual regional quality control programs.

QAS provides cross-lot data summarizing precision performance by incorporating the effect of analyte concentration. Ross and Fraser [11] and Ross and Lawson [12] have characterized the mathematical relationship between concentration and long-term within-laboratory precision for numerous analytes in the QAS program. Polynomial regression equations of CV versus concentration are used, which yield ranking of performance at the 25th, 50th, 75th, and 95th percentiles. The "CV summary" portion of Fig. 3 includes such data on cross-pool precision performance for a group of analytes.

Laboratory accreditation program (LAP)

Approximately 4,600 clinical laboratories participate in a voluntary program of laboratory accreditation sponsored by CAP [13, 14]. Volunteer teams of laboratory professionals, (i.e., pathologists, clinical scientists, medical technologists) led by a CAP member conduct on-site inspections, using comprehensive checklists which contain over two thousand key questions directed at critical structural, process, and outcome variables directly bearing on laboratory quality. Voluntary professional administration of this program is significantly achieved through regional commissioners in various geographic areas who are responsible for scheduling inspections and monitoring accredited laboratories. The LAP program of CAP is deemed to be equivalent to laboratory accreditation by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) [the primary hospital accrediting body], and licensure through the Federal Government's Health Care Financing Administration under CLIA '88.

Standards

Analytic standard solutions constitute an important link in the national reference system for clinical chemistry [15]. In this scheme, accuracy is transferred through a hierarchy of definitive, reference, and bench methods by reference materials which have been assigned highly accurate values. Through its standards program, CAP has provided standard solutions for numerous analytes, including calcium, chloride, cholesterol, ethyl alcohol, glucose, and protein, whose analytic concentrations are traceable to NBS/NIST definitive methods.

Total quality assurance-CAP Q-probes program

The CAP surveys and QAS programs relate to external and internal analytic quality control. To study and quantitate quality for process control as well as pre-and postanalytic factors, CAP has developed the Q-probes program which addresses a broad range of variables

DATA SUMMARY

ATTN
ST JOHN CLINICAL PATH LABS
22101 MOROSS RD
DETROIT, MI 48236

QUALITY ASSURANCE SERVICES

GREAT LAKES CHEMISTRY REGIONAL PROGRAM 1994

DATA SUMMARY FOR [illegible]

TOTAL FILES IN DAS 142
POSTED DATA TO 0 FILES SUMMARIZATION DATE 12/08/94
NO DATA RECEIVED FOR 142 FILES MAILING DATE 12/09/94

FILE NO.	CONSTITUENT / METHOD PRINCIPLE / INSTRUMENT/SYSTEM / UNIT OF MEASURE / LOT DESCRIPTION	LINE TITLE	YOUR LABORATORY — YOUR MONTHLY STATISTICS: LOT THRU NOV.	THIS MONTH NOV.	PREV. 1ST OCT	PREV. 2ND SEP	ALL LABORATORIES — STATISTICS OF YOUR SAME LOT AND SAME UNIT OF MEASURE: LINE TITLE	ANALYTICAL SYSTEM: LOT THRU NOV	ANALYTICAL SYSTEM: THIS MONTH NOV	METHOD PRINCIPLE: LOT THRU NOV	METHOD PRINCIPLE: THIS MONTH NOV	ALL METHODS: LOT THRU NOV	ALL METHODS: THIS MONTH NOV	COMPARATIVE METHOD: LOT THRU NOV	COMPARATIVE METHOD	ALL LOTS C.V. SUMMARY: LINE TITLE	NOV
401	GLUCOSE-SERUM	MEAN	95	NO	94	94	MEAN	98	98	98	98	99	99	98	* GLU OXIDS	LVL	REL CV
	GLUCOSE OXIDASE-COLOR	SD	2.5	DATA	1.0	1.1	SD	2.0	1.3	2.0	1.3	2.3	1.9	2.3	O2 ELECTROD	95%	4.7
	KODAK EKTACHEM 400.700	CV	2.6	RECD	1.1	1.2	CV	2.0	1.3	2.0	1.3	2.3	1.9	2.3	ALL AUTO CH	75	3.2
	MG/DL	RSLTS	93	0	24	22	FLES	37	35	41	38	238	217	31	EM INSTR	50	2.5
	XLS-88/ BX/L1	SDI	-1.49	***	-1.36	-1.60	SDI	-1.66	***	-1.49	***	-1.97	***	-1.75		25	1.9
402	GLUCOSE-SERUM	MEAN	233	NO	232	233	MEAN	237	237	236	237	243	243	241	* GLU OXIDS	LVL	REL CV
	GLUCOSE OXIDASE-COLOR	SD	2.5	DATA	1.9	1.6	SD	3.1	2.5	3.1	2.5	4.6	4.1	4.6	O2 ELECTROD	95%	4.2
	KODAK EKTACHEM 400.700	CV	1.1	RECD	.8	.7	CV	1.3	1.0	1.3	1.0	1.9	1.7	1.9	ALL AUTO CH	75	2.9
	MG/DL	RSLTS	93	0	24	22	FLES	38	36	43	39	242	220	31	EM INSTR	50	2.2
	XPS-163/BX/L2	SDI	-0.86	***	-1.05	-.89	SDI	-0.95	***	-0.86	***	-1.68	***	-2.62		25	1.7
403	SODIUM-SERUM	MEAN	153	NO	153	153	MEAN	153	153	153	153	152	152	150	ALL SODIUM	LVL	REL CV
	ISE/UNDIL KODAK ERF2	SD	1.1	DATA	1.1	1.2	SD	1.3	1.2	1.4	1.2	1.5	1.3	1.5	COMMON GP	95%	1.8
	KODAK EKTACHEM 400.700	CV	.7	RECD	.7	.8	CV	.9	.8	.9	.8	1.0	.9	1.0	ALL INSTRUM	75	1.3
	MMOL/L	RSLTS	93	0	24	22	FLES	17	15	20	17	241	221	98	ENTS	50	1.0
	XLS-88/ BX/L1	SDI	0.00	***	-.17	-.35	SDI	0.13	***	0.00	***	0.38	***	2.83		25	.8
404	SODIUM-SERUM	MEAN	131	NO	130	131	MEAN	131	131	131	131	130	130	129	ALL SODIUM	LVL	REL CV
	ISE/UNDIL KODAK ERF2	SD	1.0	DATA	.7	.8	SD	1.2	1.0	1.2	1.0	1.3	1.1	1.3	COMMON GP	95%	1.8
	KODAK EKTACHEM 400.700	CV	.7	RECD	.5	.6	CV	.9	.8	.9	.8	1.0	.9	1.0	ALL INSTRUM	75	1.3
	MMOL/L	RSLTS	93	0	24	22	FLES	17	15	20	17	242	221	97	ENTS	50	1.1
	XPS-163/BX/L2	SDI	0.09	***	-.40	-.35	SDI	0.30	***	0.09	***	0.55	***	1.87		25	.8
405	POTASSIUM-SERUM	MEAN	5.7	NO	5.7	5.8	MEAN	5.8	5.8	5.8	5.8	5.9	5.9	5.9	ALL POTASSI	LVL	REL CV
	ISE/UNDIL KODAK ERF2	SD	.10	DATA	.10	.10	SD	.12	.11	.12	.11	.09	.09	.09	UM COMMON	95%	3.2
	KODAK EKTACHEM 400.700	CV	1.8	RECD	1.8	1.8	CV	2.0	2.0	2.0	1.9	1.6	1.4	1.6	ALL INSTRUM	75	2.3
	MMOL/L	RSLTS	93	0	24	22	FLES	17	15	21	17	240	219	96	ENTS	50	1.8
	XLS-88/ BX/L1	SDI	-0.51	***	-1.12	-.38	SDI	-0.79	***	-0.51	***	-1.33	***	-1.54		25	1.5
406	POTASSIUM-SERUM	MEAN	3.3	NO	3.3	3.3	MEAN	3.3	3.3	3.3	3.3	3.3	3.3	3.3	ALL POTASSI	LVL	REL CV
	ISE/UNDIL KODAK ERF2	SD	.07	DATA	.05	.06	SD	.07	.07	.07	.06	.07	.06	.07	UM COMMON	95%	3.7
	KODAK EKTACHEM 400.700	CV	2.1	RECD	1.5	1.9	CV	2.2	2.0	2.2	1.9	2.1	1.8	2.2	ALL INSTRUM	75	2.6
	MMOL/L	RSLTS	93	0	24	22	FLES	17	15	20	17	243	223	98	ENTS	50	2.1
	XPS-163/BX/L2	SDI	-0.60	***	-.71	.30	SDI	-0.46	***	-0.60	***	-0.79	***	-0.55		25	1.7
407	CHLORIDE	MEAN	111	NO	111	111	MEAN	111	111	111	111	113	113	111	ALL CHLORID	LVL	REL CV
	ISE/UNDIL KODAK ERF2	SD	1.1	DATA	.7	.7	SD	1.0	.9	1.0	1.0	1.6	1.4	1.9	E COMMON GP	95%	2.8
	KODAK EKTACHEM 400.700	CV	1.0	RECD	.6	.6	CV	.9	.8	.9	.9	1.4	1.2	1.7	ALL AUTO CH	75	1.9
	MMOL/L	RSLTS	93	0	24	22	FLES	16	14	20	16	216	195	18	EM INSTR	50	1.5
	XLS-88/ BX/L1	SDI	-0.79	***	-.21	.01	SDI	-1.15	***	-0.79	***	-0.97	***	-0.05		25	1.2
408	CHLORIDE	MEAN	98	NO	98	98	MEAN	98	98	98	98	99	99	100	ALL CHLORID	LVL	REL CV
	ISE/UNDIL KODAK ERF2	SD	.8	DATA	.5	.6	SD	.9	.8	.9	.8	1.4	1.2	1.7	E COMMON GP	95%	2.9
	KODAK EKTACHEM 400.700	CV	.9	RECD	.5	.6	CV	.9	.8	1.0	.8	1.4	1.2	1.7	ALL AUTO CH	75	2.0
	MMOL/L	RSLTS	93	0	24	22	FLES	17	15	20	17	219	199	18	EM INSTR	50	1.5
	XPS-163/BX/L2	SDI	-0.81	***	-.17	-.01	SDI	-0.81	***	-0.81	***	-0.69	***	-0.70		25	1.2
409	CO2	MEAN	28	NO	28	27	MEAN	28.0	28.1	27.5	27.5	27.6	27.6	27.5	ALL AUTO CH		
	ENZYMATIC	SD	.9	DATA	.6	1.0	SD	1.16	1.01	1.40	1.27	1.35	1.25	1.35	EM INSTR	FILES	3328
	KODAK EKTACHEM 400.700	CV	3.1	RECD	2.1	3.7	CV	4.1	3.6	5.1	4.7	4.9	4.6	4.9			
	MMOL/L	RSLTS	93	0	24	22	FLES	30	28	101	93	196	178	196		AVG	4.5
	XLS-88/ BX/L1	SDI	0.09	***	.61	-.13	SDI	-0.42	***	0.09	***	0.10	***	0.09			
410	CO2	MEAN	15	NO	15	15	MEAN	14.6	14.7	13.7	13.8	13.8	13.8	13.8	ALL AUTO CH		
	ENZYMATIC	SD	.6	DATA	.5	.5	SD	.80	.68	.97	.87	.92	.83	.92	EM INSTR	FILES	3328
	KODAK EKTACHEM 400.700	CV	4.0	RECD	3.4	3.3	CV	5.5	4.6	7.2	6.4	6.7	6.1	6.7			
	MMOL/L	RSLTS	93	0	24	22	FLES	30	28	103	94	198	179	198		AVG	4.5
	XPS-163/BX/L2	SDI	0.82	***	1.24	.74	SDI	0.06	***	0.82	***	0.64	***	0.64			

SEE INSTRUCTION MANUAL FOR DETAILED EXPLANATIONS

Fig. 3. - Example of a laboratory's monthly QAS data summary for a group of common chemistry analytes. Cumulative data is given along with statistics from the three most recent months. Report includes general method, specific method, all-method, and comparative method comparisons, with values provided for mean, SD, CV, and SDI. Multiple lots with varying concentrations supply data for 25th, 50th, 75th, and 95th percentile rankings of performance on precision nationally, using CV-concentration polynomial regression equations solved at the laboratory's mean values for each analyte-pool combination.

important to medical care. Since 1989, data have been collected for numerous clinical laboratory quality monitors, including blood utilization for transfusion, laboratory reporting errors, cytopathology-histopathology correlation, frozen section-histopathology correlation, laboratory turnaround times, hospital nosocomial infection rates, phlebotomy complications, error rates in patient identification and appropriateness of laboratory test ordering by physicians [16]. The program complements institutional quality assurance activities, in conjunction with the JCAHO standards. In excess of one thousand hospital laboratories participate in the Q-probes program, attesting to its importance, and the level of interest it has attracted. International participation in Q-probes is growing.

Problems and challenges

Numerous problems attend the management, application, and use of quality assurance programs in the United States. These impact organizations providing programs, subscribing laboratories, and government regulatory agencies. Significant examples follow.

LOT-TO-DATE DATA
THRU NOVEMBER 1994

QUALITY ASSURANCE SERVICES

GL-SE-IL-NJ-MW-NE CROSSLINK BAXTER CHEMISTRY PROGRAM 1993-A

CONSTITUENT UNIT OF MEASURE METHOD PRINCIPLE INSTRUMENT/SYSTEM	XLS-82/BAX/L1 AVG. MEAN	XLS-82/BAX/L1 SD OF MEANS	XLS-82/BAX/L1 AVG. S.D.	XLS-82/BAX/L1 AVG. C.V.	XLS-82/BAX/L1 NO. FLS	XLS-82/BAX/L1 NO. LABS	XPS-158/BAX/L2 AVG. MEAN	XPS-158/BAX/L2 SD OF MEANS	XPS-158/BAX/L2 AVG. S.D.	XPS-158/BAX/L2 AVG. C.V.	XPS-158/BAX/L2 NO. FLS	XPS-158/BAX/L2 NO. LABS
PHOSPHORUS-SERUM MG/DL												
PHOSPHOMOL. W/ANY RED.												
ABBOTT SPECTRUM	3.63		0.21	5.8	1	1	7.81		0.33	4.2	1	1
AMERICAN MON. PARALLEL							7.69		0.17	2.2	1	1
CORNING 550 EXPRESS	3.54		0.20	5.7	1	1	7.72		0.31	4.0	1	1
GILFORD INSTRMS SYSTMS	3.12		0.18	5.7	1	1	7.88		0.40	5.1	1	1
IL MONARCH	3.44		0.19	5.5	1	1	7.64		0.29	3.8	1	1
KODAK EKTACHEM 250	3.60		0.14	4.0	2	2	7.91		0.22	2.8	2	2
KODAK EKTACHEM 400,700	3.51	0.12	0.14	3.8	41	31	7.80	0.17	0.19	2.4	41	31
KODAK EKTACHEM 500 ETC	3.55		0.19	5.1	4	4	7.80		0.23	3.0	4	4
TECH RA500,1000,XT2000	3.19		0.23	7.2	1	1	7.68		0.20	2.6	1	1
ALL AUTO CHEM INSTR	3.51	0.14	0.15	4.2	52	41	7.80	0.18	0.21	2.6	53	42
PHOSPHOMOLYBDATE UV												
ABBOTT SPECTRUM	3.44	0.08	0.17	4.9	12	11	7.48	0.13	0.25	3.3	12	11
ABBOTT SPECTRUM EPX	3.41	-	0.19	5.6	4	4	7.36		0.28	3.9	4	4
BAXTER PARAMAX	3.08	0.15	0.16	5.2	18	14	7.62	0.18	0.24	3.2	18	14
BECKMAN SY CX7/4CE/SCE	3.49		0.23	6.5	5	4	8.24		0.28	3.4	5	4
BECKMAN SYNCHRON CX4/5	3.34	0.09	0.23	6.9	7	7	8.06	0.13	0.30	3.7	7	7
BM/H 704	3.25		0.19	5.8	1	1	8.02		0.24	3.0	1	1
BM/H 717	3.17	0.11	0.16	5.1	20	18	7.87	0.18	0.25	3.1	20	18
BM/H 736	3.21	0.09	0.15	4.5	10	6	7.87	0.15	0.22	2.8	10	6
BM/H 737	3.18		0.10	3.0	1	1	7.79		0.16	2.1	1	1
BM/H 747	3.03		0.12	3.8	5	5	7.62		0.18	2.3	5	5
BM/H 911	3.25		0.19	5.6	6	6	7.91		0.26	3.3	6	6
CORNING 550 EXPRESS	3.75		0.28	7.5	3	3	7.91		0.38	4.8	3	3
COULTER OPTICHM120/180	3.62		0.29	8.0	1	1	7.87		0.40	5.1	1	1
DUPONT ACA	3.64		0.55	15.0	4	4	8.28		1.03	12.3	4	4
DUPONT DIMENSION	3.35	0.10	0.14	4.0	46	42	7.91	0.13	0.20	2.5	46	42
IL MONARCH	3.51		0.24	6.6	3	3	7.77		0.35	4.5	3	3
KODAK EKTACHEM 250	3.71		0.21	5.6	1	1	8.07		0.32	3.9	1	1
PHOSPHORUS-SERUM MG/DL												
OLYMPUS AU 5000	3.36	0.18	0.18	5.4	7	7	7.79	0.21	0.23	2.9	7	7
OLYMPUS AU 5200	3.33		0.14	4.1	1	1	7.98		0.20	2.5	1	1
OLYMPUS DEMAND	3.96		0.22	5.6	1	1	8.42		0.32	3.8	1	1
OLYMPUS REPLY	3.06		0.30	9.6	4	4	7.71		0.44	5.7	3	3
ROCHE COBAS FARA/MIRA	3.00	0.28	0.22	7.2	16	14	7.60	0.32	0.30	3.9	16	14
TECH RA500,1000,XT2000	3.49		0.23	6.7	5	5	8.16		0.30	3.7	6	6
TECHNICON DAX	2.81		0.10	3.6	1	1	7.94		0.14	1.8	1	1
ALL AUTO CHEM INSTR	3.28	0.23	0.18	5.5	182	151	7.83	0.27	0.26	3.4	182	152
ALL METHOD PRINCIPLES ALL AUTO CHEM INSTR	3.33	0.24	0.18	5.2	234	191	7.82	0.25	0.25	3.2	235	193

STATISTICS FROM "ALL" GROUPINGS OF FEWER THAN 3 ARE EXCLUDED

EACH FILE CONTAINS 10 OR MORE LOT-TO-DATE RESULTS

Fig. 4. - CAP Quality Assurance Service (QAS) Regional Quality Control Program data summary from two pools of control serum. Example indicates data for inorganic phosphorus, and includes average data file mean, SD, and CV, SD of file means, and numbers of files and laboratories.

Limited characterization of performance by proficiency testing

Because clinical laboratories are highly complex, their objective assessment should be based on multiple descriptors characterizing a wide variety of performance variables. From the simplistic regulatory perspective, PT, through EQA quantitates measurable variables, and therefore becomes a tempting yardstick. PT alone, however, significantly fails to detect poorly performing laboratories and creates false signals of unacceptability in good laboratories, (i.e., alpha and beta error) [17]. A combination of programs for external quality assessment, internal and extended internal (regional) quality control, total quality assurance, and inspection is superior to any single measuring device to characterize and quantitate performance [18].

The quantitative inter-relationships between such programs have been studied in a preliminary fashion. We have documented that laboratories inspected through the CAP LAP program obtained significantly fewer unacceptable PT results on glucose, potassium, inorganic phosphorus, and aspartate aminotransferase. In addition, for a cohort of laboratories, we have verified only moderate degrees of correlation between bias, precision, and total error as determined in surveys and QAS, for the above analytes [18]. The clinical laboratory profession must work to discourage overreliance on PT as the sole or dominant factor used to assess participant performance.

System international (SI) units

A full discussion of SI units is beyond the scope of this presentation. There has been slow implementation of SI units in North American clinical laboratories, where this requires changes in traditional units for common analytes. The CLIA '88 regulations include significant sanctions applied to laboratories that are unsuccessful in PT [7]. In a study of proficiency testing failures at the Mayo Clinic by Klee and Forsman, only a minority of unacceptable results were found to be caused by laboratory analytic problems. Sixteen percent were attributable to clerical error [19]. Any requirement that reporting for surveys be in units other than those used for the daily reporting of medical data to physicians increases the opportunity for clerical error.

QAS provides reporting in either conventional or SI units. Data is integrated accordingly, through appropriate interunit conversions. Surveys accept data from a mix of conventional and SI units, based on needs of foreign participants. The surveys program allows full SI units under special circumstances. A more comprehensive program for flexible unitage is under development. Any full conversion of surveys to SI units must be managed intelligently, with careful attention to the needs and risks by participating laboratories, respecting the regulatory environment.

Logistics

Management of surveys require contracting for, purchasing, and coordination of packaging and shipping of supplies; maintenance and improvement of computer hardware, software, and data bases; data solicitation, entry, verification, reduction, and reporting; control of committee and staff functions; and interrelating with affiliated organizations and government licensing entities. As the numbers of surveys, participants, analytes, and specimens increase from year to year, the logistics of providing an EQA program which meets all government's required characteristics, and remains useful to the participant, become increasingly challenging and prone to problems.

Matrix effect

Analytic materials used for external and internal quality control should be similar to patient specimens insofar as possible. To the extent that manufacture introduces changes rendering these materials different in their reactivity than patient specimens, matrix effects are present. Controls must be stable, available in sufficiently large uniform lots to accommodate multilaboratory usage, and free as possible from matrix effect. Laboratory and method comparisons in surveys and QAS should ideally reflect relative performance which would have been obtained with patient specimens. Thus, matrix effect becomes particularly problematic when it causes certain methods to behave idiosyncratically. In the hematology surveys, it has now become necessary to use seven different materials specific for various groups of integrated automated WBC differential analyzers, as no control material is uniformly applicable to all devices (Table 3).

Method-specific (peer group) evaluation of surveys substantially eliminates matrix effect as an artifact of grading. For methods subject to matrix effects, grading remains problematic. This applies to analytes graded by comparative method and with peer groups too small to generate reliable target values and/or limits. CAP, through its industry liaison committee, is working with manufacturers of clinical laboratory devices and control products to characterize and quantitate matrix effect and to develop materials which behave as closely as possible to patient specimens. An analysis of matrix impact on EQA is provided in proceedings of a dedicated CAP conference [20].

Target value validation

The use of definitive methods to quantitate unknown analytes in survey material is costly and time consuming. Thus, the numbers of pools and analytes receiving this validation has been limited. Within the framework of the

national reference system for clinical chemistry, there will be a shift to greater use of less costly reference methods traceable to definitive methods, to facilitate more widespread and comprehensive analysis of survey and QAS pools.

Nontraditional laboratories

Advances in technology have yielded reasonably reliable measuring devices for use outside of the traditional clinical laboratory. Such analyzers are commonly employed in physician offices, and also in hospital locations such as out-patient care areas, the bedside, and in the surgical suite. They frequently are operated by individuals with minimal formal laboratory training. Professional EQA programs have been predominantly directed at hospital and independent laboratories. Survey philosophy, analyte configuration, grading criteria, control products, and instructional and evaluation materials need to be re-evaluated to accommodate this evolution in testing. CAP has chosen to develop surveys for nontraditional laboratories in cooperation with other interested professional organizations, where appropriate, as indicated above.

Surveying multiple methods within a laboratory

Frequently, laboratories test for the same analyte by multiple methods using different reagent systems and instruments. This reflects factors such as location, (e.g., outpatient, inpatient, central, remote), acuity, (e.g., urgent *vs* routine), or workload (e.g., multiple simultaneous analyses). EQA traditionally challenges by analyte and therefore fails to sample error conditions of all participants' testing environments. Either PT programs need to expand to test all methods used in laboratories, or intralaboratory linkage between various methods must be defined, quantitated, and incorporated into evaluation schemes. CAP is addressing this problem through the use of overlapping and duplicated surveys, and through shared pools (CrossLink controls) linking external and internal quality control.

Commercial use of survey data

Survey data provide a means to compare aspects of performance of reagent systems and instruments. However, this statistical information also reflects the variables of matrix effect and laboratory quality, and furthermore may vary in time across multiple challenges. From time to time, certain commercial vendors have attempted to use CAP survey summarized data reports (Fig. 2) to imply superiority or inferiority of given testing products. Because of the above limitations, CAP does not permit use of the data in this manner. A detailed copyright statement addressing this issue is included with each group data summary.

All conclusions and interpretations in this article, with respect to the College of American Pathologists data, are those of the author and not those of the College.

Submitted on invitation.
Accepted on 6 February 1995.

REFERENCES

1. BELK, W.P. & SUNDERMAN, F.W. 1947. A survey of the accuracy of chemical analyses in clinical laboratories. *Am. J. Clin. Pathol.* **17**: 853-861.

2. RIPPEY, J.H. 1987. Proficiency testing. In: *Laboratory quality assurance*. P.J. Howanitz & J.H. Howanitz (Eds). McGraw-Hill, New York. pp. 317-333.

3. GILBERT, R.K. 1978. Accuracy of clinical laboratories studied by comparison with definitive methods. *Am. J. Clin. Pathol.* **70**: 450-470.

4. HARTMANN, A.E., NAITO, H.K., BURNETT, R.W. & WELCH, M.J. 1985. Accuracy of participant results utilized as target values in the CAP chemistry survey program. *Arch. Pathol. Lab. Med.* **109**: 894-903.

5. DERMAN, H. & DORSEY, D.B. 1991. The pathology of regulation. *Clin. Lab. Med.* **11**: 793-802.

6. UNITED STATES. 1990. Medicare, Medicaid and CLIA Programs. Revision of the laboratory regulations for the medicare, medicaid, and clinical laboratories improvement act of 1967 programs. *Fed. Reg.* **55**(50): 9538-9610.

7. UNITED STATES. 1992. Clinical laboratory improvement amendments of 1988; final rule. *Fed. Reg.* **57**(40): 7137-7288.

8. LAWSON, N.S. & HAVEN, G.T. 1976. The role of regional quality control programs in the practice of laboratory medicine in the United States. *Am. J. Clin. Pathol.* **66**: 268-275.

9. ROSS, J.W. & LAWSON, N.S. 1987. Performance characteristics and analytic goals. In: *Laboratory quality assurance*. P.J. Howanitz & J.H. Howanitz (Eds). McGraw-Hill, New York. pp. 124-165.

10. LAWSON, P.L., LAWSON, N.S. & ROSS, J.W. 1995. The stability of target values when survey assayed control materials are used in a regional internal quality control program. The CAP chemistry-QAS shared pool experience. *Arch. Pathol. Lab. Med.* **119**: 312-333.

11. ROSS, J.W. & FRASER, M.D. 1982. Clinical laboratory precision: the state of the art and medical usefulness based internal quality control. *Am. J. Clin. Pathol.* **78**: 578-586.

12. ROSS, J.W. & LAWSON, N.S. Analytical goals, concentration relationships and the state of the art for clinical laboratory precision. *Arch. Pathol. Lab. Med.* (in press).

13. DUCKWORTH, J.K. 1987. Laboratory licensure and accreditation. In: *Laboratory quality assurance*. P.J. Howanitz & J.H. Howanitz (Eds). McGraw-Hill, New York. pp. 334-353.

14. BATJER, J.D. 1990. The College of American pathologists laboratory accreditation programme. *Clin. Lab. Haemat.* **12** (Suppl. 1): 135-138.

15. VANDERLINDE, R.E., BOWERS, G.N., SCHAFFER, R. & EDWARDS, G.C. 1989. The national reference system for cholesterol. *Clin. Lab. Med.* **9**: 89-104.

16. HOWANITZ, P.J. 1990. Quality assurance measurements in departments of pathology and laboratory medicine. *Arch. Pathol. Lab. Med.* **114**: 1131-1135.

17. EHRMEYER, S.S. & LAESSIG, R.H. 1988. An evaluation of the ability of proficiency testing programs to determine intralaboratory performance. *Arch. Pathol. Lab. Med.* **112**: 444-448.

18. LAWSON, N.S., GILMORE, B.F. & THOLEN, D.T. 1988. Multiprogram characterization of laboratory bias, precision, and total error. *Arch. Pathol. Lab. Med.* **112**: 454-461.

19. KLEE, G.G. & FORSMAN, R.W. 1988. A user's classification of problems identified by proficiency testing surveys. *Arch. Pathol. Lab. Med.* **112**: 371-373.

20. *Matrix effects and accuracy assessment in clinical chemistry.* 1993. College of American Pathologists Conference XXIII. W.G. Miller & H.W. Kaufman (Eds). *Arch. Pathol. Lab. Med.* **117**: 343-436.