

Managing the Pre- and Post-analytical Phases of the Total Testing Process

Robert Hawkins, M.D.

Department of Laboratory Medicine, Tan Tock Seng Hospital, Tan Tok Seng, Singapore

For many years, the clinical laboratory's focus on analytical quality has resulted in an error rate of 4-5 sigma, which surpasses most other areas in healthcare. However, greater appreciation of the prevalence of errors in the pre- and post-analytical phases and their potential for patient harm has led to increasing requirements for laboratories to take greater responsibility for activities outside their immediate control. Accreditation bodies such as the Joint Commission International (JCI) and the College of American Pathologists (CAP) now require clear and effective procedures for patient/sample identification and communication of critical results. There are a variety of free on-line resources available to aid in managing the extra-analytical phase and the recent publication of quality indicators and proposed performance levels by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) working group on laboratory errors and patient safety provides particularly useful benchmarking data. Managing the extra-laboratory phase of the total testing cycle is the next challenge for laboratory medicine. By building on its existing quality management expertise, quantitative scientific background and familiarity with information technology, the clinical laboratory is well suited to play a greater role in reducing errors and improving patient safety outside the confines of the laboratory.

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Corresponding author: Robert Hawkins
Department of Laboratory Medicine,
Tan Tock Seng Hospital, 11 Jalan Tan Tock
Seng 308433, Singapore
Tel: +65-6357-8943
Fax: +65-6235-6507
E-mail: Robert_Hawkins@tsh.com.sg

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INTRODUCTION

In recent years, there has been increasing interest in quality improvement and patient safety activities in healthcare. The clinical laboratory has a leader in the field of healthcare quality management with a focus on analytical quality born of its scientific background and was one of the first areas to use quantitative statistical control methods. However laboratories are now being asked to widen their focus to consider activities outside their immediate control. Accreditation agencies are increasingly requiring laboratories to go beyond analytical quality and take responsibility for the pre- and post-analytical (or extra-analytical) phases where most errors arise. These new challenges are a change from the traditional laboratory-based activities with which many laboratory

staff is comfortable and this new role can cause some unease and discomfort. This article outlines the different phases of the total testing process, discusses laboratory accreditation requirements for the extra-analytical phase and describes some of the resources available for laboratories in managing this unfamiliar area.

1. The total testing process (TTP)

The total testing process (or total testing cycle) is based on the original brain-to-brain loop concept described by Lundberg [1, 2]. He outlined a series of activities, starting with the clinical question in the clinician's mind, leading to test selection, sample collection, transport to the laboratory, analysis, reporting back to the clinician, and final interpretation and decision making by the

clinician. These activities have traditionally been separated into three phases (pre-analytical, analytical and post-analytical). Some authors have introduced the “pre-pre-” and “post-post-” analytical phases to identify activities associated with the initial selection of tests and with the interpretation by clinicians respectively, to differentiate them for the pure collection/transport activities (pre-analytical phase) and reporting (post-analytical phase) [3, 4]. There is some evidence that these steps are more error-prone than other pre- and post-analytical activities [3-8]. However, the definition and use of such terms is not universal. Indeed the definition of even basic terms such as pre-analytical, analytical and post-analytical can vary between authorities.

2. Errors in the total testing phase

Healthcare is a relatively high risk area and the overall defect rate in healthcare in the United States is estimated to be 31-69% [9]. Error rates are often described using the sigma concept, which refers to the number of standard deviations that lie between the process mean and the specification limit. As the process standard deviation becomes smaller, more standard deviations will fit between the mean and the specification limit, increasing the sigma number and decreasing the likelihood of items exceeding the specification limit. Using this measure, healthcare performs at a 1-2 sigma level, which compares poorly with non-healthcare industries such as airline baggage handling (approximately 4 sigma) [9]. Performance varies in different areas of healthcare, with values of 1 sigma (e.g., use of beta-blockers post myocardial infarction, detection and management of depression) to 3 sigma (e.g., adverse drug events, hospital-acquired infections). Higher error rates can be expected in institutions under pressure to increase revenue, lower costs and operate close to or over full capacity [10].

The analytical phase of laboratory medicine is arguably the best performing sector in healthcare with close to 5 sigma performance (0.002%) [9, 11]. This is more than 3,000 times lower than the rates of infection and medication errors and reflects the standardised quantitative nature of much of laboratory medicine testing, which is well suited to statistical quality control measures [12]. However, the accomplishments of laboratory medicine drop when errors in all phases of the total testing process are considered [13, 14]. The proportion of errors associated with the two extra-analytical phases is 4-5 times that seen in the analytical phase, with the pre-analytical phase consistently representing over half of all errors in published studies [12, 15-19]. In a representative study, an Italian stat laboratory used the same methodology to assess error rates in 1996 and 2006 and

found that, despite a 34% reduction in error rate, the pattern of 62% pre-analytical, 15% analytical and 23% post-analytical phase errors remained basically unchanged [20]. Given the high volumes of laboratory tests performed globally, even a low prevalence of errors translates into significant absolute numbers of occurrences and opportunities for adverse patient outcome. Although some laboratories have developed mechanisms to detect errors and improve pre- and post-analytical quality, there remains significant room for improvement in the quality of the extra-analytical testing phase [21-23].

The commonest causes of errors in the total testing process as compiled by Plebani are shown below [22].

1) Pre-pre-analytical (46-68%)

Inappropriate test request, order entry, patient/specimen mis-identification, sample collected from infusion route, sample collection (hemolysis, clotting, insufficient volume, etc.), inappropriate container, handling, storage and transportation.

2) Pre-analytical (3-5%)

Sorting and routing, pour-off, aliquoting, pipetting and labeling, centrifugation (time and/or speed).

3) Analytical (7-13%)

Equipment malfunction, sample mix-ups, interference (endogenous or exogenous), undetected failure in quality control.

4) Post-analytical (13-20%)

Erroneous validation of analytical data, failure in reporting/addressing the report, excessive turn-around-time, improper data entry and manual transcription error, failure/delay in reporting critical values.

5) Post-post-analytical (25-46%)

Delayed/missed reaction to laboratory reporting, incorrect interpretation, inappropriate/inadequate follow-up plan, failure to order appropriate consultation.

These lists illustrate the use of the pre-pre- and post-post-analytical categories - note, for example, that Plebani includes choice of container, collection, handling and transportation as pre-pre-analytical activities, resulting in most errors being categorised as pre-pre-analytical rather than pre-analytical. The lack of standardisation in such taxonomy accounts for some of the variation seen in reported error rates and can complicate discussions [24]. However, the concepts may have value in shap-

ing the laboratory's approach to error management by acting as an explicit reminder of the error-prone nature of test selection and interpretation activities [25].

Errors in healthcare are of concern when they lead to actual or potential adverse outcomes for patients. Given the complex nature of healthcare and the difficulty in assessing the effect of a specific laboratory error on patient management, the prevalence of proven patient harm is difficult to assess. Obvious extreme errors in qualitative results with clear links to therapy or management decisions (e.g., histopathology, blood transfusion, microbiology, virology, genetic testing) are easiest to measure but assessing the effect of quantitative errors in clinical biochemistry and haematology results is much more difficult. Such difficulties mean that present measurements probably significantly underestimate the size of the problem in light of the high volume of quantitative testing performed in clinical laboratories. A review of the available literature on laboratory errors found great heterogeneity in the studies where the data collection method appeared to be the strongest influence on error prevalence and type [19]. Published data suggest that 24-30% of laboratory errors have an effect on patient care while actual or potential patient harm occurs in 3-12% [20, 22, 26]. Some areas, such as molecular genetics testing, can have actual harm rates of up to 100% [19, 27]. A recent study illustrating the dichotomy between the large potential for harm but the much smaller rate of actual harm describes a five-point scoring system for actual and potential adverse impact score elements [28, 29]. Errors were classified as pre-analytical (88.9%), analytical (9.6%) and post-analytical (1.5%). Classification and grading of quality failures in the clinical biochemistry laboratory showed that 72.7% of errors had an actual adverse impact score of 1 (least severe grade) while 65.9% of errors had a potential adverse impact score of 5 (most severe grade) [28].

Although the importance of the pre- and post-analytical phase has been acknowledged for many years, laboratories have often overlooked this area in their quality management programmes, focussing instead on analytical quality and associated activities within their direct control. The main reason for this neglect has been governance issues due to the variety of the different physical locations and staff groups (laboratory staff, clinicians, phlebotomists, porters) involved in the total testing process. Ignorance by non-laboratory staff of the importance of the extra-analytical phase, difficulties in capturing appropriate monitoring data, taxonomical issues in defining and classifying errors and narrow interpretations of the laboratory's role have all contributed to this inaction. The variety of different terms used to de-

fine errors, including mistakes, blunders, defects, outliers, unacceptable results, quality failures, have not helped discussion [22]. The term "laboratory error" is defined in International Organization for Standardization (ISO) 22367 as "failure of planned action to be completed as intended, or use a wrong plan to achieve an aim, occurring at any part of the laboratory cycle, from ordering examinations to reporting results and appropriately interpreting and reacting to them" and is the preferred term [22, 30]. A more recent and perhaps more useful description of laboratory error is "any defect from ordering tests to reporting results and appropriately interpreting and reacting on these" [31]. Recent changes to accreditation requirements are forcing laboratories to pay attention to this area.

3. Accreditation requirements for the extra-analytical phase

The present interest in patient safety initiatives can be traced to studies in the 1990s showing that up to 4% of patients in the United States suffered iatrogenic injuries, of which two-thirds were mistakes [32, 33]. Even higher rates were noted in Australia (13%) and the UK (10%) [34, 35]. A series of publications in the US and UK between 1999 and 2004 subsequently led to greater requirements for active management of the extra-analytical phase of the total testing process [36-39]. The Institute of Medicine reports "To Err is Human: Building a Safer Health System" (1999) and "Crossing the Quality Chasm: a New Health System for the 21st Century" (2001) described the high rates of medical error in hospitals in the United States and outlined strategies to reduce their incidence. While the first report highlighted the many American patients who die each year from medical errors, the second described six aims for patient care, specifically safeness, effectiveness, efficiency, equitability, patient-centeredness, timeliness, and rules for care delivery redesign. Medical errors were defined as the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim. The majority of medical errors was not the result of individual recklessness or the actions of a particular group but was caused by faulty systems, processes, and conditions that led people to make mistakes or fail to prevent them. Amongst the strategies proposed were the raising of performance standards and expectations for improvements in safety through the actions of oversight organizations and professional groups and the implementing of safety systems in healthcare organizations to ensure safe practices at the delivery level.

These recommendations have been translated in new specific requirements to enhance patient safety by US-based accreditation bodies with similar provisions in other international stan-

dards. They can also be found in voluntary guidelines such as those of the National Quality Forum whose 2009 publication "Preferred Practices for Measuring and Reporting Patient Safety and Communication in Laboratory Medicine" focuses on the same areas of patient/sample identification, sample acceptability, test order accuracy, verbal communication and critical result reporting targeted by the accreditation bodies described below [40].

1) Joint Commission International

The Joint Commission International (JCI) is a subsidiary of The Joint Commission (TJC), formerly the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). TJC is a United States-based not-for-profit organization that accredits over 19,000 healthcare organizations and programs in the United States while JCI accredits healthcare organizations in over 80 countries. On-site inspections follow a three cycle. JCI requires all accredited organizations to implement the JCI International Patient Safety Goals (IPSGs) under the International Standards for Hospitals [41]. The purpose of the IPSGs is to promote specific improvements in patient safety. There are six goals, of which the first two specifically refer to the extra-analytical phase of the total testing process.

The first Standard IPSG 1 requires the organization to develop an approach to improve accuracy of patient identification and applies to the pre-analytical phase of the total testing process. Of all the pre-analytical processes, sample collection is arguably the most critical [42, 43]. Identification errors can result in inappropriate treatment and mislabeling of blood specimens may result in hemolytic transfusion reactions from incompatible blood [44, 45]. Up to 50% of transfusion-related deaths result from identification error [46-49]. Up to 1 in 18 identification errors can result in an adverse patient outcome [50]. Identification errors are particularly common amongst inpatient samples [51]. Identification processes when giving blood, or blood products or taking blood and other specimens for clinical testing are specifically highlighted by JCI. Patients must be identified using at least two ways, such as name, identification number, birth date or bar-coded wristband. The patient's room number or location cannot be used for identification purposes. Evidence of implementation of this system for blood and blood product administration and clinical sample collection are amongst the measurable elements for this goal.

IPSG 2 requires the organization to develop an approach to improve the effectiveness of communication among caregivers and applies to both the pre- and post-analytical phases of the total testing process. Verbal and telephone requests (pre-analytical

phase) and the reporting back of critical test results (post-analytical phase) are specifically mentioned as areas for action. Critical values are defined as those which represent potentially life-threatening situations and in which reporting delays can result in serious adverse patient outcomes [52-57]. Policies or procedures are required for verbal and telephone orders that includes the writing down (or entering into a computer) of the complete order or test result by the receiver of the information; the reading back of the order or test result; and confirmation that what has been written down and read back is accurate. Although not all laboratories accept verbal or telephone requests, all will report critical results and thus need to comply with this requirement. Evidence of writing down, reading back and confirmation of verbal/telephone requests and critical results are the measurable elements for this standard.

The importance of pre-analytical processes and critical result communication are reiterated in AOP (Assessment of Patients) standard 5.6, requiring procedures for test ordering and sample collection, identification, transport, storage, preservation, receipt and tracking, and AOP 5.3.1, which requires a collaborative method to be used to develop processes for reporting of critical results, respectively [58].

2) College of American Pathologists Laboratory Accreditation Program

The College of American Pathologists (CAP) Laboratory Accreditation Program is an international program designed to improve patient safety by advancing the quality of pathology and laboratory services through education, standard setting, and ensuring laboratories meet or exceed regulatory requirements. More than 6,000 laboratories worldwide are CAP accredited. Inspections are carried out by teams of practicing laboratory professionals using checklists which cover general laboratory functions as well as specific disciplines. The checklist questions are explicit in their intent and the required evidence of compliance (e.g., records, written procedures and policies).

The Laboratory General Checklist specifically refers to the monitoring of extra-analytical quality and the CAP laboratory patient safety goals [59]. Item GEN.20316 requires the quality management program to include monitoring key indicators of quality. Pre-analytical examples given include patient/specimen identification (e.g., percent of patient wristbands with errors, percent of ordered tests with patient identification errors, or percent of results with identification errors), test order accuracy (e.g., percent of test orders correctly entered into a laboratory computer), specimen acceptability (e.g., percent of general hematology

and/or chemistry specimens accepted for testing), surgical pathology/cytology specimen labeling (e.g., percent of requisitions or specimen containers with one or more errors of pre-defined type), and blood culture contamination (e.g., percent of blood cultures that grow bacteria that are highly likely to represent contaminants). Post-analytical examples given include critical value reporting (e.g., percent of critical results with documentation that results have been reported to caregivers, percent of critical results for which the primary clinician cannot be contacted in a reasonable period of time) and stat test turnaround time (either collection-to-reporting turnaround time or receipt-in-laboratory-to-reporting turnaround time of tests ordered with a stat priority). Turnaround time potentially encompasses all three phases of the total testing process and can be an excellent single measure of laboratory performance.

Items GEN.20348 and GEN.20364 deal with monitoring of pre-analytical and post-analytical processes, respectively, and again list examples of pre-analytical (accuracy of transmission of physicians' orders, specimen transport and preparation, requisition accuracy, quality of phlebotomy services, specimen acceptability rates) and post-analytical measures (accuracy of data transmission across electronic interfaces, reflex testing, turnaround time from test completion to reporting and interpretability of reports) measures. A written quality management plan listing the processes to be monitored and defining the criteria used to monitor these processes as well as records of monitoring data with review and comparison to benchmark data/defined thresholds is required.

Item GEN.20365 requires the laboratory to specifically address the four CAP Laboratory Patient Safety Goals, all of which refer to the extra-analytical phases. The first two match JCI IPSGs 1 and 2. The first goal requires the laboratory to improve patient and sample identification at specimen collection, analysis and result while the second refers to improvement of verification and communication of life-threatening or life-altering information regarding malignancies, HIV (and other serious infectious diseases), cytogenetic abnormalities, and critical results. In line with the emphasis on patient safety and a holistic multidisciplinary approach to quality management, the third goal is to improve identification, communication and correction of errors in a timely manner while the fourth is to improve the coordination of the laboratory's patient safety role within healthcare organizations (nursing, administration, point-of-care personnel and providers). Again records of evaluation or monitoring of processes related to each of the patient safety goals are required.

Other items in both the Laboratory General and discipline-spe-

cific checklists refer to pre- and post-analytical processes. For example, GEN.40490 requires the individual collecting a specimen to positively identify the patient prior to specimen collection using at least 2 identifiers. GEN.40491 requires primary specimen containers to be labeled with at least 2 identifiers. GEN.40535 and 40540 require quality management system for problems in specimen transport, including from remote sites and those not under the control of the laboratory. GEN.41320, 41330 and 41340 reinforce the procedures and monitoring of critical result handling with similar requirements restated in the discipline-specific checklists (e.g., CHM.15100 and 15200 in the Chemistry and Toxicology checklist).

3) ISO 15189: 2007 Medical laboratories - Particular requirements for quality and competence

The ISO 15189:2007 standard is designed for use by medical laboratories in developing their quality management systems and assessing their own competence, and for use by accreditation bodies in confirming or recognising the competence of medical laboratories [60].

Although ISO 15189:2007 covers all three phases of the total testing process, it is less prescriptive and explicit in managing and monitoring of extra-analytical quality issues compared to the JCI and CAP standards. For example, section 4.2.2 on the quality management (QM) system states that "the QM system shall include, but not be limited to, internal quality control and participation in organised inter-laboratory comparisons such as external quality assessment schemes". A list of 23 items for inclusion in the quality manual mentions transportation, collection, handling of samples, reporting of results and communications and other interaction with patients, health professionals, referral laboratories and suppliers in passing (item 4.2.4) while the monitoring programme describes calibration and function of instruments, reagents and analytical system (item 4.2.5). Monitoring of turnaround time as part of the management review is required (item 4.15.2 k) as is monitoring of the transportation of samples to the laboratory with respect to time frame, temperature, preservatives and safety (item 5.4.6). "External quality assessment programmes should, as far as possible, ... have the effect of checking the entire examination process, including pre- and post-examination procedures" (item 5.6.4). Procedures and records of critical result handling are required (items 5.8.7 and 5.8.10) and the definition of critical results should be decided locally in agreement with the clinicians using the laboratory (item 5.8.8). This provides an opportunity to both customize critical value reporting to clinician needs and educate physi-

cians in the concept of critical values [61].

The increasing recognition of the importance of the extra-analytical phases in laboratory medicine is seen not only in accreditation standards from outside authorities but also in the recent deliberations of laboratory quality experts. In May 2010, a meeting of over 40 medical laboratory opinion leaders met to discuss issues and current challenges for laboratory medicine [62]. One working group looked at assessment of risk and control of sources of error in the laboratory path of workflow. They considered two recently published CLSI risk management guidelines relevant to extra-analytical quality concerns and examined two specific questions in this area [63, 64]. The first question was “What factors, activities or conditions in the total testing process contribute to risk of harm to the patient?” Using the CLSI document on management of non-conforming laboratory events, the group identified the following activities: ordering the test, sample collection, sample labeling/patient identification, sample transport, sample accession/handling processing, and sample quality (pre-analytical phase); and result interpretation (including calculation errors), data entry, and transmission and communication of results (post-analytical phase) [65]. It was felt that the most problematic area in risk management is tackling the human factor in the process. The second question was “Because even one bad result issued by a virology laboratory or blood bank may compromise both patient health and laboratory credibility, how should labs manage risk in these laboratories? Are there any specific special precautions?” Responses included the need to gain cooperation from all stakeholders, to standardize and simplify processes, to use technology wherever possible, to validate the steps in the TTP and continually monitor activities in the TTP to implement quality improvement.

Both the laboratory quality experts and the accreditation authorities recognize that laboratory medicine is a complex process whose management requires careful integration between

different physical sites, activities and occupational groups to minimize the risk of error occurrence. This is illustrated in the Swiss cheese model of error propagation of Reason [22, 66]. A system is a series of processes which can be considered analogous to a stack of slices of Swiss cheese in which the holes represent opportunities for an error to pass to the next process in the system. Each slice is a defensive layer and can stop the error from propagating through the system. The vulnerability of the system is dependent on the number of defensive layers and their efficiency [67]. Errors can result in adverse patient outcome when all the holes line up and the system fails to detect and rectify the error. For laboratory medicine, the slices represent areas such as equipment, training, supervision and quality assurance procedures and there is a need to close the gaps and strengthen the defenses to minimize the likelihood of patient mishap. Management strategies should recognize both the human and the system factors that can lead to errors and should aim for a robust integrated system which provide timely intervention and correction of developing problems.

Table 1 compares the definitions of the pre- and post-analytical processes used in CAP (items GEN.20348 and 20364) with the equivalent terms (pre- and post-examination procedures/pre- and post-analytical phase) used in ISO 15189:2007 (items 3.10 and 3.11) [59, 60]. The pre-analytical definitions are very similar but there are some differences in the post-analytical areas, with ISO 15189:2007 including “authorization for release” and “storage of samples” as post-analytical activities. These definitions illustrate the difficulties that can be encountered in discussions on extra-analytical phase errors and accounts for some of the variation in reported error rates.

4. Free resources available for managing the extra-analytical phase

There are a variety of free on-line resources available to the lab-

Table 1. Comparison of pre-analytical and post-analytical phase definitions [59, 60]

Phase	CAP Laboratory General Checklist	ISO 15189:2007
Pre-analytical	All steps in the process prior to the analytic phase of testing, starting with the physician's order. Examples include accuracy of transmission of physicians' orders, specimen transport and preparation, requisition accuracy, quality of phlebotomy services, specimen acceptability rates, etc.	Steps starting, in chronological order, from the clinicians request and including the examination requisition, preparation of the patient, collection of the primary sample, and transportation to and within the lab and ending when the analytical examination procedure begins.
Post - analytical	All steps in the overall laboratory process between completion of the analytic phase of testing and results receipt by the requesting physician. Examples are accuracy of data transmission across electronic interfaces, reflex testing, turnaround time from test completion to chart posting (paper and/or electronic), and interpretability of reports.	Processes following the examination including systematic review, formatting and interpretation, authorization for release, reporting and transmission of results and storage of samples of the examinations.

Abbreviations: CAP, College of American Pathologists; ISO, International Organization for Standardization.

oratory seeking background information and suggested procedures for pre-analytical phase procedures. Manufacturers of laboratory sample containers are also a valuable source of reference and educational material which can be tailored to the specific collection and analytical equipment used by a particular laboratory. The following is an incomplete list of sites and publications (both commercial and non-commercial) that provides free information in this area. At present there is unfortunately little on-line information on the post-analytical phase.

1) The Quality of Diagnostic Samples. This is an on-line interactive version of the publication of the same name from the Working Group on Pre-analytical Quality of the German Society for Clinical Chemistry and Laboratory Medicine [68]. It provides general recommendations on sample collection as well as information on individual analyte sample collection requirements and stability.

2) World Health Organisation - Use of anticoagulants in diagnostic laboratory investigations 2002 [69]. Although almost a decade old, this document provides similar information on individual analyte collection requirements and stability to the "Quality of Diagnostic Samples" site but in a single printable document.

3) Specimenscare.com - a global pre-analytics resource centre [70]. This website aims to provide a single global resource of data and educational material on the pre-analytical phase. There is a wide variety of materials available, including posters, presentations and flowcharts.

4) Educational materials on blood sample and urine collection [71, 72].

5) Educational material on blood gas and capillary sample collection [73].

6) Educational material on general pre-analytical quality [74].

Until recently, there has been little available information on quality indicators in laboratory medicine. A review of laboratory quality indicators could find an evidence base for only 14 indicators of which 10 were extra-analytical: test order appropriateness, wristband identification errors, patient satisfaction with phlebotomy, specimen quality, availability of inpatient results, corrected laboratory reports, critical value reporting, turnaround time, clinician satisfaction and follow-up of abnormal cervical cytology [56]. Many of the indicators in common use by laboratories suffer from inconsistency in definition, measurement methodologies and reporting practices and a general lack of basic supporting evidence. Even the denominator (per patient, per sample, per test) used in reporting rates of errors can vary between authors [19].

In recent years, several national and regional external quality assurance programmes to examine extra-analytical quality have been developed [75-78]. The approach with the greatest potential global utility is that of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Working Group on "Laboratory errors and patient safety" (WG-LEPS), which has published preliminary benchmarking data for all phases of the analytical phase [79-81]. The working group's mission is to stimulate studies on the topic of errors in laboratory medicine, to collect available data and to recommend strategies and procedures to improve patient safety. One of their projects has been to create a systematic common reporting system for clinical laboratories based on standardised data collection, and to define state-of-the-art and quality specifications for each quality indicator independent of the size of organization and type of activities, complexity of processes undertaken, and different degree of knowledge and ability of the staff. A website is available for data submission (www2.csinet.it/mqiweb/) and the working group recently published the results of data collected from 39 laboratories (25 from Europe, 3 from USA, 3 from Asia-Pacific, 8 from elsewhere) from February 2008 to December 2009.

The quality indicators for the pre- and post-analytical phase together with the proposed standards are shown in Table 2. Although zero defects are the ultimate goal, the quality standards suggested represent "state of the art" performance. In some cases, a single quality criterion is given due to the low value observed in the study while in other, no value is given due to the small number of laboratories responding obtained and the wide range of values reported. In terms of the JCI and CAP patient safety goals regarding sample identification and handling of critical results, the table classifies performances of <0.4% misidentified samples, <50 min average time for critical result communication, and >96% critical result communication as meeting optimum levels. It should be appreciated that these are preliminary goals reflecting the heterogeneous group of laboratories around the world contributing to the data collection exercise. For laboratories that already exceed these levels, an expectation of even higher performance may be more appropriate. For example, a CAP Q-Tracks study of 180 institutions showed the 25% best performing laboratories had reported critical result rates of >99% in 2001, a level probably driven by US regulatory requirements [82]. There are differences between US and European practices, particularly with respect to the notifier and the choice of critical values [83, 84]. The laboratory's focus on internal versus external activities also appears to vary between the US and the UK, with greater attention to implementation of clini-

Table 2. Proposed Pre-analytical and Post-analytical Quality Specifications from IFCC Working Group Project “Laboratory Errors and Patient Safety” [81]

	Performance level			
	Optimum	Desirable	Minimum	Unacceptable
Pre-analytical Quality Specifications				
% requests with clinical question from general practitioners/total number of requests from general practitioners	>87	58-87	29-57	<29
% appropriate requests, with respect of clinical question from general practitioners /number of requests that reports clinical question from general practitioners	>97	65-97	32-64	<32
% requests without physician identification/total number of requests	<5	5.0-6.0	6.1-8.0	>8.0
% unintelligible requests/total number of requests	<0.2	0.20-0.25	0.26-0.30	>0.30
% requests with errors concerning patient identification/total number of requests	<0.4	0.40-0.50	0.51-0.60	>0.60
% requests with errors concerning physician identification/total number of requests		<0.1		
% requests with errors concerning input of tests (missing)/total number of requests	<0.3	0.30-0.40	0.41-0.50	>0.50
% requests with errors concerning input of tests (added)/total number of requests		<0.1		
% requests with errors concerning input of tests (misinterpreted)/total number of requests	<0.2	0.20-0.25	0.26-0.30	>0.30
% samples lost-not received/total number of samples	<0.2	0.20-0.40	0.41-0.60	>0.60
% samples collected in inappropriate container/total number of samples	<0.07	0.07-1.13	1.14-0.20	>0.20
% samples hemolysed (chemistry)/total number of samples	<1	1.0-1.5	1.6-2.0	>2.0
% samples clotted (hematology)/total number of samples with anticoagulant	<0.5	0.50-1.0	1.1-2.0	>2.1
% samples with insufficient sample volume/total number of samples	<0.4	0.40-0.80	0.81-1.20	>1.20
% samples with inadequate sample-anticoagulant/total number of samples with anticoagulant	<0.2	0.20-0.30	0.31-0.40	>0.40
% samples damaged in transport/total number of samples		<0.1		
% samples improperly labelled/total number of samples	<0.07	0.07-0.15	0.16-0.20	>0.20
Post-analytical Quality Specifications				
% reports delivered outside the specified time/total number of reports	<0.4	0.4-0.5	0.6-0.7	>0.7
% critical values communicated/total number of critical values to communicate	>96	77-96	58-76	<58
Average time to communicate critical values (min)	<50	50-100	101-160	>160

Abbreviation: IFCC, International Federation of Clinical Chemistry and Laboratory Medicine.

cal guidelines, test utilisation and result interpretation by physicians in the UK [85]. Nevertheless these criteria represent excellent starting points for laboratories in setting benchmarks for extra-analytical quality monitoring and are a significant step forward in developing consensus standards [86]. The group plans to eliminate and modify some existing indicators and develop new ones over the next year [81]. The project’s success depends on the participation and collaboration of laboratories enrolled in the project to help define best practice and improve performance and laboratories interested in participating are encouraged to contact the group through the website mentioned above.

Another source of information on present practices in quality indicator monitoring is a recent article describing the results of a survey of members of the Association of Clinical Biochemists in the United Kingdom, which elicited responses from 335 individ-

uals [85]. The author lists 11 questions as pre-analytical, 5 as analytical and 7 as post-analytical, although their classification would not necessarily match the CAP and ISO 15189:2007 phase definitions discussed earlier. Most laboratories had an electronic handbook (84%), provided help and advice in interpreting clinical laboratory data (80%) and discussed turnaround times with clinical staff (75%) but only 58% had a written critical limits (alert) list. This is a useful snapshot of quality practices in UK laboratories and highlights some of the areas where improvement is required.

5. Priority areas for extra-analytical quality

Review of the accreditation criteria, patient safety concerns and discussions in the literature suggest some clear areas for action for laboratories looking to expand their quality focus outside the

physical confines of the laboratory. The two areas of highest priority are patient/sample identification (pre-analytical quality) and the handling of critical results (post-analytical quality). For many laboratories, attention to these issues is required by regulation or patient safety goals and for the remainder, they are becoming part of the good laboratory practices expected of all laboratories worldwide. A variety of approaches, both procedural and information technology-based, are now available for laboratories seeking guidance [24, 83, 87].

The next step could be to expand these items to include more of the testing process. In the pre-analytical area, laboratories can develop clear sample acceptance and rejection criteria which are linked to monitoring of the collection and transport processes. Sample haemolysis and clotting are the commonest causes of unsuitable blood specimens and most laboratories have procedures to handle such specimens at sample receipt, but a more pro-active approach extending back to the point of collection is required [26, 50, 88]. The laboratory's procedures regarding unlabelled or mislabelled specimens should be clear and sample relabeling by laboratory personnel, clinical staff or third parties is strongly discouraged [67]. Collection procedure, container, transport temperature/time/safety and within-laboratory pre-analytical temperature/time/safety criteria should be stipulated and monitored. In the post-analytical area, attention to critical result reporting can be expanded to include all reports, ensuring that the right report goes to the right clinician within the right timeframe. This could include monitoring of the wider definition of turnaround time from test request to clinician review commonly used by clinicians, rather than the traditional sample receipt to result reporting approach favoured by many laboratories [19, 89-91].

Laboratories looking to incorporate the pre-pre- and post-post-analytical phases into their management plans may wish to monitor the appropriateness of test requesting and utility of interpretative reporting. Duplicate laboratory requests repeated within defined intervals can represent wasted and unnecessary testing [92-95]. Repetition of tests can result from poor access to previous results or lack of standardisation between different laboratories [96]. Given the suggestion that up to 50% of requests may be inappropriate, introducing strategies to manage duplicate testing can be a useful first step in initiating demand management without challenging the autonomy of clinical decision makers [97]. Information technology, such as electronic medical records, clinician order entry, expert systems, electronic handbooks and embedded hyperlinks in reports, is probably the easiest way to both provide solutions and monitor performance in

these phases [98-100]. Clinical audits and clinician satisfaction surveys can also be useful measures of overall laboratory effectiveness [43, 101].

SUMMARY

For many years, the clinical laboratory has been at the forefront of quality improvement activities in the healthcare sector. Its focus on analytical quality has resulted in an error rate of 4-5 sigma which surpasses most other areas in healthcare. However, greater appreciation of the prevalence of errors in the pre- and post-analytical phases and their potential for patient harm has led to increasing requirements for laboratories to take greater responsibility for activities outside their immediate control. Accreditation bodies such as JCI and CAP specifically require healthcare organisations to have clear and effective procedures for patient/sample identification and communication of critical results and to monitor their performance in these areas. There are a variety of free on-line resources available to aid in managing the extra-analytical phase and the recent publication of quality indicators and proposed performance levels by the IFCC WG-LEPS provides useful benchmarking data for laboratories embarking on extra-analytical quality improvement programmes. Managing the extra-laboratory phase of the total testing cycle is the next challenge for laboratory medicine. By building on its existing quality management expertise, quantitative scientific background and familiarity with information technology, the clinical laboratory is well suited to play a greater role in reducing errors and improving patient safety.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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