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Review Article

DETECTION AND PREVENTION OF DIAGNOSTIC ERROR IN CLINICAL CHEMISTRY LABORATORIES: REVISITED

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ABSTRACT

Interest in laboratory error was heightened with the publication of the Institute of medicine (IOM) report in 2000: To Err is human; however, there is still a neglect on the problem of error. Beside causing serious harm to patients, medical errors translate into huge costs for the national economy. This article demonstrates that pre and post analytical steps of the total testing process (TTP) are prone to error than the analytical phase. In the interest of patient any direct or indirect negative consequence related to the clinical laboratories must be considered. International ideas should identify areas of quality improvement. Redesigning the system will help prevent error.

INTRODUCTION

Clinical chemistry as an essential arm of laboratory medicine develops and utilizes chemical concepts, procedures and techniques in investigations which pertain to understanding, diagnosis, therapy of disease and assessment of health (Paul, 1975). This goal is attained through diligent analysis of specimens from human subjects. The nature of the information required may seek to answer any one or more of the questions relating to the pathological entity (a) screening the population for the selection of at risk subjects. (b) Diagnosis of a pathological state. (c) Classification and/or sub-classification of a pathological state (d) Determination of the prognostic index as well as the relative risk in the population (e) Monitoring the efficacy of the treatment modality. In general, clinical chemistry laboratory conducts in-vitro analysis of biochemical constitution of a subject, in order to determine specific information correlated with in-vivo metabolism.

The recent interest in diagnostic error in clinical chemistry laboratories were preceded during the past decade by a focus on the problem solving strategies of the experts of that time. This focus also extended to include the development of computer based decision support systems to aid clinicians in diagnosis. This interest was heightened, since the Institute of Medicine (IOM) published report, To Err is Human, an alarming data on the cause and impact of medical error (Kohn *et al.,* 2002).

However, there is still a relative neglect of the problem. Besides causing serious harm to patients, medical errors can affect national economy. In 2006, Null and Colleagues published an article indicating the overall estimated annual lost of improper medical intervention approaching $282 billion in United State (Null *et al*., 2006) While many areas of health care are still struggling with the issue of patient safety, clinical laboratory medicine has always been a frontier in pursing this

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issue since they are involved in promoting research, education and professional development in clinical laboratory medicine, patient safety is finally the object of medical and public attention (Kohn *et al.,* 2000) The awareness and understanding of medical errors have spread rapidly, with a determination to promote safety movement promoting safer health care through solution strategies. The cause of diagnostic errors and preventable deaths was not careless or incompetent people but bad system (Leape, 2009). When compared with other types of medical errors, diagnostic error received little attention and the reasons for this neglect are complex as in (table I).

Table 1 Error in Clinical Chemistry Laboratories: reasons for neglect

1. Lack of universal consensus on the definition of laboratory errors.
2. Difficulties in discovering and identifying all types of errors as result of split specimen design.
3. Numerous step that stretches across multiple providers.
4. Negative connotation of blame
5. Laboratorian not whiling to report and disclose data on type of error and the frequency
6. Increasing use of point of care and near patient monitoring system

Most of the many different terms used to define error in laboratory medicine (eg blunders, outliers, defects, unacceptable result and failure) have negative connotation and a sense of blame, individual failure and pertain to studies focusing on a limited number of total testing process (TTP) steps. The lack of a universally accepted definition of error and above all of "allowable error rate", reduces the possibility of evaluating the impact of laboratory error on patient outcomes. The main step toward achieving reduction in errors and improve patient safety in laboratory medicine will be made once univocal consensus has been reached on comprehensive definition and evaluation of error in laboratory testing. Errors in clinical laboratory are difficult to identify and when found are less easily understood than other types of medical error. Compared with adverse events related to other treatment errors that are easily discovered (e.g medication, surgery), laboratory errors tend to be more harmful and difficult to identify in time. The difficulties depend largely on several steps that are involved. Firstly, there is a time lapse between laboratory testing, clinician's action and patient outcomes. These failures in the process steps to patient intervention are likely to result in patient harm. Failures that occur earlier on the process are likely to result in process disruption but "active and passive" defensive barriers – which rely on science and technology, people, procedures and administrative controls s– may soften their potential effect or may prevent the recognition of their effect on the final adverse event.

Secondly, the testing process is complex, consists of many steps and extend across multiple providers. All the phases of the total testing process can be targeted individually for improving quality, although it is well published that most errors occur in pre-and post analytical phase (table 2a and 2b) (Plebani 2007, Stankovic and Romeo 2007). Only the analytical phase falls under laboratory control, while the pre-analytical and post analytical phases pertain to different set of providers other than laboratory staff such as the clinician, the nurse, the patient and others involved in patient identification, Bio-data entry, specimen collection and transport.

Many factors affect test results, before laboratory analysis occurs, these include sex, age, race, medication, haemolysis, compliance to pre-testing instructions, physiological state, and circadian rhythm. Based on these factors, laboratory test results must be interpreted in context of the overall health of the patient. Bonini and Colleagues documented that pre-analytical error predominated in the laboratory, ranging from 31.6% to 75% (Stankovic and Romeo 2007). Chawla and colleagues reported during their 1-year study (2008-2009) in clinical chemistry on the frequency of pre-analytical errors observed in both inpatients and outpatients. For the inpatients, a pre-analytical error rate of 1.10% and outpatient, the error rate was 1.2%, and the variable with the highest frequency rating was insufficient volume for testing (Julie, 2012). In the post-analytical phase, results are released to the clinician and she/he interprets them and makes diagnostic and therapeutic decisions. There is the possibility of inappropriate response to laboratory test result, interpretation and critical result reporting are areas of potential error (Boone, 2004). Carefully designed works, a multidisciplinary approach and team work are therefore required for a careful investigation of TTP. Plebani and Piva give a comprehensive overview on the ongoing effects for improving actual consensus on the definition and notification of laboratory critical values, and for evaluating their contribution to improve clinician outcomes and patient safety and also on a valuable experience of automated notification, which is a reliable tool for improving the timeliness of communication and avoiding potential errors which accreditation programs require read-back of the result (Plebani, 2009).

Thirdly clinicians responsible for making decisions at times perceive laboratory errors as a harmful source of patient injury, nor do they understand that most laboratory error mistakes may arise from pre-and post analytical steps. Fourthly, laboratory scientist are not willing to make known the data on the frequency and types of errors observed in their own setting for fear of blame, individual failure and guilt associated with these events (Okane, 2004).

This makes it difficult to analyse the entire testing process and set quality standard operation processes for each step in order to identify weakness in policies and procedures to provide opportunity for quality improvement through the formulation and prioritization of corrective actions. Finally, laboratory testing is no longer done only in the clinical laboratory setting, point-of-care testing, the fastest growing sequent of current clinical laboratory testing, near patient testing used for self-monitoring are widely alternative and complementary testing options. There is an urgent need to evaluate errors in the laboratory within the reliable frame work of the total testing process (TTP). From the patient's view point, the integrity of the entire process is necessary and there is a need to prevent any error in the pre-intra or post analytic phase. From this perspective, any possible mistakes in TTP should be investigated in order to prevent any negative impact on patient care, irrespective of the step involved, and of whether the error has been caused by a laboratory scientist (eg calibration or analysis) or by a non-laboratory operator (eg inappropriate test request, error in patient identification, blood collection eg

haemolysis and result interpretation (Plebani 2006, Plebani 2007).

Table 2a Types and Rates of Errors in the 3 stages of laboratory testing process reference[5]

Phase of Total Testing process	Type of Error	Rate
Pre-analytical	inappropriate test request Order entry error Misidentification of patient Wrong contained Sample collection and transport Inadequate sample/anticoagulant volume Ratio, insufficient sample volume sorting and Routine errors labeling errors.	46%-68.2%
Analytical	Equipment malfunction sample mix-ups/interference, undetected failure in quality control procedure not followed.	7%-13%
Post analytical	failure in reporting erroneous validation of analytical data improper data entry.	18.5%-47%

Table 2b Frequency and type of errors according to the phases of TTP

Total	Absolute frequency ppm		Relative frequency (%)	
	1996	2006	1996	2006
Total errors	4667	3092		
Preanalytic	3186	1913	68.2	61.9
Analytic	617	646	13.3	15.0
Postanalytic	864	715	18.5	23.1

Definition of laboratory error

Our search revealed large heterogencity in different study designs and quality on this topic as well as relatively few data and the lack of a univocal definition of "Laboratory error" (also reffered as "blunder", "Mistake", "problem" 'defects', 'outliers' 'unacceptable result', quality failure) have almost exclusively all the evaluation of analytical error or, as in the case of the split-specimen design, are insensitive to many steps in the testing process, particularly those at the beginning and at the end of the cycle. Despite these limitations, there was considerable concordance on the distribution of errors throughout the laboratory working process. One recent and interesting proposal made is to use a neutral term such as "quality failure", which soften the negative connotations associated with earlier reported terms, and that sense of blame. According to the authors, this term means any failure to meet the required output quality necessary for optimum patient care anywhere in the process pathway from test selection to the return of an appropriately interpreted report to requesting clinicians (Okane, 2004). This definition has a clear focus on patient care and outcomes rather than on processes and procedures. However, the term 'error' is used in the medical literature, and should therefore be used also for errors in laboratory medicine, particularly as they are part of the broader issue of diagnostic error (Plebani, 2009).

The Technical specification released by international organization for standardization (ISO/TS 22367) defines laboratory error 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 (ISO/TS 2008).

This comprehensive definition encourages a patient centered evaluation of errors in laboratory testing. It has been emphasized that the promotion of patient centered care should be translated into the need to investigate any possible defect that occurs in the TPP and may have a negative impact on the patient. Any direct or indirect negative consequence related to laboratory test must be considered, irrespective of whether the source lies in the pre, intra, or post analytic phase; it is, irrelevant whether an error has been caused by laboratory professional (eg standardization, calibration or testing error) or by a non-laboratory operator (eg Patient/Specimen misidentification inappropriate test request or interpretation (Plebani, 2007). TTP is the framework for considering and identifying laboratory errors, both for testing in 'traditional" clinical laboratories and with point-of-care testing (POCT) or alternative testing types (devices for near-patient resting and self-monitoring).

Sources of errors in clinical chemistry laboratory and their prevalence

Clinical laboratory; as a specialty set high quality control, has always been at the forefront of error reduction.

In terms of quality control and error rates, laboratory medicine has a far better record than most other fields of health care. Regulation of quality in the health care sector is based on accreditation, certification, quality monitoring, patient's rights, standard operation procedures and standards of health care quality (Zima, 2010). Some studies indicate that, in the analytic phase, the average error rate is low as 0.002%; this is functioning at the five sigma level. As a comparison, the rates of infections and medication errors are closer to three stigma, that is defects rates > 3000-fold those in clinical laboratory. The concept of "sigma" according to stringent strict statistical quality control criteria, means that a process is considered to be in control if the variation expressed as standard deviation (Sigma δ) is less than 1/6 of the difference between the process mean and the control limit(Hinckley, 1997). Errors related to laboratory testing are too common and constitute a significant fraction of diagnostic errors in medicine today. Laboratory testing in modern clinical medicine is assuming an increasingly important position in the diagnostic process, and in monitoring the effect of therapy. Therefore, even a low incidence of laboratory testing errors among the millions of laboratory investigations performance every day throughout the world might have important health and patient safety consequences. Data collected on laboratory error rates will depend on the study design and in particular the total testing steps investigated. It is therefore easy to understand why the error rates may vary every 33-50 events to 1000 events or from 214 to 8300 laboratory results (Mcswiney and Woodrow 1969; Trevor *et al.,* 2015, Khawy *et al* 1996, Lapworth and Teal 1994).

Analytical errors

Analytical phase begins when the patient specimen is prepared in the laboratory for testing, and it ends when the test result is verified by a clinical scientist or Pathologist. Early studies in the field of error in clinical laboratory were devoted to identifying analytical errors. The analytical processes are under the control of the laboratory staff and is the 'core' of laboratory work. An analysis of the data collected and reported in the

literature, starting with the paper published by Belk and sunderman in 1947 through the result collected by the college of America pathologists in the 90s and, finally the data published by Witte and co workers in 1997 showed that error rates have decreased from 162,116per million laboratory test (part per million, ppm) to 447 ppm (Bonin *et al* 2002; Belk and Sunderman 1947; Steindel *et al.,* 1996).

The impressive reduction in errors, by about 300- fold are derived from improving analytical quality by establishing well defined rules for internal quality control (IQC) and external quality assessment (EQA), automation, assay standardization, improved laboratory technology, and better trained staff. The role of EQA and Proficiency testing (PT) is to provide reliable information allowing laboratories to assess and monitor the quality status of internal procedures and processes.

The suitability of the diagnostic system, the accountability and competence of the staff along with the definition of measurement uncertainty in the laboratory results have also contributed greatly. The responsibility of laboratory professionals is to appropriately analyse EQA/PT samples and reports, defect trends or bias that may not be apparent in single results, investigate root causes producing unacceptable performances, apply and monitor opportune actions for removing and determine whether the problem affected clinical decision making (Howanitz, 2005).

However, recently collected data demonstrate that analytical quality is still a major issue. Westgard has demonstrated that estimates on a δ scale for common clinical chemistry and coagulation test are not satisfactory, ranging from 3 to 4δ, at best. Unsatisfactory analytical performance has been described not only in the field of clinical chemistry, but also in haematology, coagulation and molecular biology test (Westgard and Westgard 2006). In particular, a relatively high frequency of analytical error has been documented for immunoassay with associated adverse clinical outcomes. In some cases, analytical interference in immunoassay has resulted in grossly erroneous results (Tate and Wara 2004, Ismail 2009). Recently data collected on the interference of para proteins in many laboratory measurements, including glucose, bilirubin, C-reactive protein, creatinine, albumin and Uric acid demonstrate that the frequency of this type of error is variable and underreported (Dalal and Bridgen 2009). In addition, it has been reported that haemolysis still causes factitiously high biochemical parameter levels, thus stressing the need for more appropriate guideline for the identification and appropriate treatment of unsuitable specimens (Lippi *et al.,* 2008).

Therefore, despite the impressive improvement achieved in analytical quality, evidence demonstrates that further improvements are needed. This should be achieved by setting down and using evidence based analytical quality specification in every day practice, and rules for internal quality control and external quality assessment procedures would be more appropriate. However, there is an urgent need for standard programmes aiming at improving traceability and correcting biases and systematic errors, finally, more stringent metrics, such as the six sigma should be introduced into clinical laboratories to improve upon current analytical processes.

Pre- and Post analytical phases

The pre-analytical phase of the total laboratory testing process is where the majority of laboratory errors occur. Pre-analytical errors can occur at the time of patient assessment, test order entry, request completion, patient identification, specimen collection, specimen transport or specimen receipt in the laboratory. While the frequency of laboratory errors varies greatly, depending on the study design and TTP steps investigated. Papers published between 1989 and 2007 and another documented between 2008 to 2009 drew the attention of laboratory professionals to the pre- and post analytical phases, which currently appear to be more prone to errors than the analytical phase (Plebani 2007). In three papers published between 1997, 2007 and 2012, using one study design to investigate most TTP in the same clinical context; the pre analytical phase had the highest error rate, the frequent problems arising from mistakes in tube filling, inappropriate containers and requesting procedure. The main reasons for errors in the post-analytic phase were on excessive turnaround time in the study, errors in keyboard and missed correction of erroneous finding in the former studies but thanks to improved information procedures, and ward identification. Further studies confirm that the pre- and post-analytical phases are much more error-prone than analytical phase (Astion *et al.,* 2003; Kalra 2004).

Pre-pre and Post-Post analytical Steps

As pointed out by Lundberg with the concept of brain to-train loop in 1981, laboratory professionals were not concerned enough about the initial and final TTP steps, namely the appropriateness of test requesting, patient and specimen identification and the clinicians reaction to the report, interpretation and use of the results (Lundberg 1998; Lundberg 1981). It shows that these steps performed neither in the clinical laboratory nor at least under the control of laboratory professional, are more error prone than other (Laposata and Dighe 2007) Recent data on errors in the pre-pre analytical phase-procedures -performed neither in the clinical laboratory nor under the control of laboratory professional that failures to order appropriate laboratory tests, accoutered for 55% observed incidents of missed and delayed diagnosis and 58% of errors in the emergency ward (Stroobants *et al*., 2003, Hickner *et al*,. 2008, Gandhi *et al* 2007, Casalino *et al*., 2009). In the final steps of the loop, the incorrect interpretation of laboratory result was found to be responsible for a high percentage of error in the ambulatory and as well as in emergency department (table 3).

A recent study noted that failure to inform outpatients of significant abnormal test result appear to be common; examples include patients not being informed of results of total cholesterol as high as 9.1mmol/L [3.5-6.5], blood glucose level as high as 10mmol/L (3.6-5.6) and a potassium level as low as 2.8mmol/L (3.5-5.0). The overall rate of failure to inform the patient of record/document communication of information was 7.1% ranging between practices from 0% to 26% (Casalino *et al*., 2009). This failure to inform patients of abnormal results hinders a move away from traditional role of clinicians towards a new model incorporating shared decision making in which the clinician attempts to provide the patient and guardian with the full range of information including laboratory results, about

the clinical condition (Hartzband and Groopman, 2009). Another evidence of laboratory errors in reacting to laboratory information is given in a study on the prescription of potassium despite the presence of hyperkalemia (Schiff *et al*., 2000). The above data demonstrate that the initial and final steps of the TTP process, in particular test requesting and reaction to laboratory results, not only are more error-prone than all the other steps, but are more important causes of potential adverse outcomes for patients.

Errors in point of care testing (POCT) and alternative site testing

Data on errors in POCT are scanty, the main focus being only on analytical error, the claimed advantage of POCT, in addition to its reduced turnaround-time is that it calls for fewer steps in producing laboratory results and errors originating during transport are reduced and post-analytical errors are practically total eliminated since results are presented directly to the care-giver (Drenk, 2001). This in turn, should reduce associated errors. However, despite the simplicity of the operation, POCT devices are affected by several environmental and operator related factors. Managing the pre, intra and post analytic processes is a major challenge in POCT, just as it is in main laboratories. Recently analysed errors and patient safety problems related to POCT adopting a modified kost error classification framework that takes into account all steps of the testing process, thus demonstrating that POCT reduces errors and risks of error only in a few steps of the entire testing process (Kost 2003 and Plebani 2009). Furthermore POCT has given rise to new and serious problems particularly to operator impotence and non-adherence to procedures. A potentially most dangerous possibility is that the rapid availability of results and immediate therapeutic intervention might amplify the clinical impact of errors and translate into adverse events for patient (Jones and Merer 2004, Merer and Jone 2005). Recently a significant number of errors in data transcription and incomplete data were reported using glucose meters in the hospital setting, thus stressing the possibility of post-analytical phase when using POCT (Cararo and Plebani 2009). While these errors do not arise in the laboratory, they pertain to the utilization of result by provides the unique framework for analyzing and reducing errors and the risk of errors, not only in centralized laboratory testing but also in POCT and all other alternative site testing option.

Table 3 Post-post analytical errors: frequency of incorrect interpretation of diagnostic tests in different clinical settings

Setting	primary care	Emergency medicine	Internal department
Incorrect interpretation of diagnostic tests: estimate (%)	37	38	37
References	36	73	74

Effect of errors in Clinical laboratories

A small proportion of laboratory errors results in patient harm and adverse events but thanks to the several barriers and defensive layers present between the release of laboratory information the decision making process and the action of the patient. The data published in the literature on effect of laboratory error on patient (Table 4).

The risk of adverse events and inappropriate care due to laboratory errors ranges from 2.7 to 12%, while in a large percentage of cases (24.4% to 30%). In a published studies error resulted in inappropriate admission to intensive care units (Plebani and Cararo 1997). The impact of laboratory error on the patients as regards further inappropriate investigations and more invasive testing and additional consultations is much higher and although not necessarily harmful, creates discomfort and incurs high costs for both patients and the health care system. From a risk management view point, the great majority of laboratory errors with little direct impact on patient care provide important learning opportunities. In fact, any error, might indicate weakness in policies and procedure that may not lead to adverse events in their particular context but might cause the patient harm in slightly different way. Therefore, a suitable pattern of grading laboratory errors according to their seriousness should help identify ways for quality improvement and focus corrective/preventive measures the grading system would be designed to consider not only the real patient harm effect sustained but also the potential worst-case scenario if such an error were to reoccur (Okane *et al.,* 2008).

Table 4 Impact of errors in laboratory medicine on patient outcomes

Authors (Reference)	Number of errors	Effect on patient care (%)	Adverse events or risk of adverse events (%)
Ross JW	336	30	7
Nutting PA	180	27	12
Plebani M	189	26	6.4
Carraro P	160	24.4	2.7

Adopted from Annals of Clinical Biochemistry volume 47 March 2010: 102-109

According to the ISO Technical specification the medical laboratories reduction of error through risk assessment and continual improvement any clinical laboratory must implement processes for

(a) Identifying high-risk process where the potential error could lead to a safety risk for patient, (b) Identifying actual incidents associated with deviations from standard procedure;(c) Estimating and evaluating the associated risks to patient safety, (d) Controlling these risk and (e) Monitoring the effectiveness of the control undertaken (ISO/TS, 2008). In addition to the ISO/TS 2236, a proposal, with several advantages, suggests that it is possible to assign both an actual (A) and a potential (P) score to describe the seriousness of an individual laboratory scoring system based on patient outcome (Okane, 2004). These data demonstrate the laboratory errors may play a significant role in patient safety.

Approach of error and ways to improve patient safety

The human error, especially error in clinical laboratories can be viewed in three ways; the person, the legal and system approach (Reason, 2000).

Personal approach

The longstanding and widespread way of the personal approach focuses on the unsafe act, errors and procedural violations of individuals at sharp end: nurses physicians, anaesthetists, pharmacists, surgeons, and in some cases, laboratory professionals. It views unsafe act as arising from mental processes such as poor motivation, carelessness, forgetfulness,

inattention, negligence and recklessness. Some measures, directed mainly at reducing unwanted variability in human attitude include disciplinary measures, litigation, retraining, blaming and shaming. The personal approach the main tradition in clinical laboratories, has serious shortcomings: it precludes a detailed analysis of mishaps, incidents, near-misses and isolates unsafe acts from their system context, thus precluding an effective risk management policy (Leape and Fromson 2006).

Legal approach

According to this model, responsible professionals should not make mistakes as this part of the duty of care such mistakes are limited but sufficient to cause adverse events to patients. Errors with negative consequences are considered due to negligence or even recklessness and therefore call for punitive measures. From this perspective, the connection between proximal actions and bad outcomes is far easier to prove than that between organizational issues and management decisions. The convenience for lawyers in chasing individual errors rather than collective ones is further reinforced by the willing of professionals, including physicians, to accept responsibility for their actions and the drawbacks of this model is that best people make mistakes or errors. It prevents any planned design to disclose medical errors. Hospitals fear public disclosure of reports, which damage reputation and cause loss of patients and litigation, while expert agree that a voluntary system for the reporting of medical errors and adverse events has great potential for improving safety (Gostrin 2000 and Leap 2002). The legal approach encourages defensive medicine which can, in the laboratory setting, translate into excessive and inappropriate testing, thus leading to excessive cost and related inefficiencies.

System approach

The system approach bears the notion that humans are fallible and errors are to be expected, even in the best possible organizations. These errors are caused by organizational problem outside the laboratory and related to other frequent error in healthcare. Errors, seen as consequences rather than causes, originate in systemic factors, including recurrent error traps in the world place and the organizational processes that give rise to them. Countermeasures are based on the assumption that although the human condition cannot be changed, the human conditions under which humans work can be improved upon. In particular, defence, barriers and safeguards occupy a central role in this approach. The quantitatively largest reductions in error are likely to result from interdepartmental cooperation designed to improve data dissemination.

High-technology system, including clinical laboratories have many defensive layers but sometimes they have so many holes like slices of cheese and the holes in the numerous layer may line up to permit a trajectory of accident opportunity, bringing hazards into damaging contact with victims (Reason 2000).

The practice of in the clinical laboratories as highly complex. Of the factors linked to the complexity of TPP, the most significant are the several steps, and the different professionals involved in these steps, which are only partically under the control of the laboratory professionals. The model accepted to the specific setting of clinical laboratory focus on the most important gaps, and defence layers, the most effective of which are the identification and documentation of all processes and procedures, automation and simplification, adequate personnel training, supervision and quality indicators.

According to this plan, the ability to detect the incipient indicators and the collective will to implement corrective measures are essential prerequisites of an effective risk management programme. Process control and proactive hazards analysis tools such as FMEA (failure mode and effect analysis). HACCP (hazards analysis and critical control points) and HAZOP (hazards and operability studies) have already demonstrated their effectiveness in identifying weakness in laboratory processes and minimizing the risk of error (Chiozza 2009, Bakker and Muke 2007, Signori *et al.,* 2007).

Reduction of errors in clinical laboratories

An increasing body of evidence demonstrates that the analytical error rate has improved significantly over time (Leap 2002). In addition to efforts aiming to reduce analytical errors and improve quality, important achievements have been made in addressing errors in clinical laboratories with the introduction of pre-analytical workstations, a significant reduction has been achieved in pre-analytical errors in the automation of procedures such as specimen preparation centrifugation, aliquoting, pipetling and sorting (Holman *et al*., 2002 and DaRing 2009) The increasing interest shown in developing guidelines, blood collection, sample handling and specimen acceptance or rejection will translate into higher quality standard (Lippi *et al*., 2006, Lippi *et al.,* 2006, Lippi and Guide 2007, Lippi *et al.,* 2007). Modern robotic technologies and information systems can also help reduce pre-analytical errors. Computerized order entry simplifies test ordering and eliminates a second person from transcribing the order. Automated phlebotomy tray preparation provides a complete set of labeled blood tubes and the tables for hand labeling in a single tray for each patient. Pre-analytical robotic workstations automate some of the steps and reduce the number of manual steps involving more people, Pal Bela and Colleague also simplify specimen routing and tracking ((Pat Bela and Lars 2009). Automated computerized communication systems have recently been developed to improve the timeliness of notification and avoid potential error for which accreditation programme required read back of the result. After being validated by pathologist on call, critical values are automatically communicated to the clinicians in real time short messages appearing on desktop computers (Piva *et al.,* 2009 and Plebani *et al.,* 2009).

These IT system, which improve the likelihood of reaching the pathologist on call are easily adapted to reach patient on their desktop computers thereby representing an effective means of reducing or eliminating the failure to communicate abnormal outpatient test results to users. Further initiative concern the introduction of more effective automated procedures for data validation and reporting as well as the implementation of systems which allows are effective knowledge management to support data interpretation and clinical decision-making at the point of care (Oosterhiuis *et al*., 2000) this can include a direct link into the laboratory handbook giving guidance on interpretation as well as the procedural information required to

carry out investigation on individual patient (Kay, 2006). Similar tools should be used to improve the appropriateness and documented procedures through proactive tools such FMEA and HAZOP have already proven effective in reducing the risk probability index and, therefore improving patient safety in laboratory testing (WHO, 2008). There proactive tools are accepted by laboratory professionals and clinicians because they exploit professional competences through a positive approach to problems by focusing on the examination of the entire testing process, thus anticipating major adverse events to prevent them.

International Ideas to reduce errors in clinical laboratory

The World Alliance for patient safety in 2004 included the communication of critical test results among potential safety solution topics, thus acknowledging the importance of avoiding errors in laboratory testing (WHO, 2008) The second goal of joint commission 2008 National Patient Safety Goals for Laboratories is to improve the effectiveness of communication among care givers, the first goal being to improve accuracy of and final steps of the testing process (International Patient Safety Goal, 2007). The working group on laboratory error and patient safety (WG-LEPS) of the international federation of clinical chemistry and laboratory medicine (IFCC) has initial a project named model of quality indicators based on the identification of valuable and univocally accepted quality indicators in all steps of the testing process. Currently, 25 quality indicators were selected after analysis made by 26 clinical laboratories enrolled in the working group: 16 for the pre-analytical, 3 for the analytic and 6 for the post analytical phase.

According to the development, laboratories that were involved may introduce the data collected in their own institution on each and all quality indicators in a specifically developed website (www.3centroricerca biomedica.it). Initial analysis of the collected data has been made and reported, but more data are needed to allow for a well defined statistical analysis (Scianocorelli and Plebani 2009). Other steps of the projects are (a) to define preliminary quality specifications for each quality indicator; (b) to assess the data with respect to the preliminary quality specifications; (c) to re-evaluate the quality specification and to implement an external assurance programme by which participating laboratories may evaluate their performances on the basis of a comparison between the results obtained and the desirable quality specification identified for each indicator. The aim of the programme, therefore is to encourage each clinical laboratory to assess and monitor its own performance not only in its analytic aspects but also in the pre-and post analytic phases and also, it should be possible to identify and monitor error rates in TTP and to improve upon the process on the basis of objective and quality specifications defined by the scientists all over the world. There is need to establish a reliable policy of adoption of a sentinel event in clinical laboratories.

A sentinel events is an unexpected occurrence involving death or serious physical or psychological injury, or the risk thus showing the need for immediate investigation and response. There is urgent need to settle universally agreed "laboratory unexpected events" throughout the total testing process, which could allow gaining important information about serious incidents and holding both providers and stakeholders accountable for patient safety.

Some of these sentinel events have already been identified, including inappropriate test requests and patient misidentification (pre-analytical phase), use of wrong assays for critical diseases (eg Myocardial infarction) severe analytical errors, critical test like electrolytes performed on unsuitable samples. (eg haemolysed sample), the release of laboratory results in spite of poor quality control results, the failure to alert critical values and the wrong report destination (Lippi *et al*., 2009). This tragic event cause by a human error, once again demonstrated weakness in the system and holes in the defensive layers. Taking into account, current international ideas and suggestions, "some priority areas of improvement in patient safety and in error reduction in clinical laboratory as table5.

Table 5 Priority areas of patient safety involvement in laboratory medicine

1	Accuracy of patient/specimen identification
2	Effectiveness of laboratory data communication by laboratorian
3	Communication of critical test results urgently
4	Sample acceptability and rejection definition criteria
5	Appropriateness of test request by clinician

CONCLUSION

Significant progress has been made since the release of "To Err is Human" in reduction of error in medicine. Those involved are aware that, rather than being caused by bad people, error are indicative of weaknesses of the system, a system that includes almost all the processes and methods we use to organize and carry out everything we do in medicine, including laboratory medicine.

The first lesion we learnt is, therefore, that the system theory works and that errors and their effects can be prevented by redesigning systems so as to make it difficult for care-givers to make mistakes. In laboratory, process analysis, the recording/documentation of all procedures and processes according to quality standards particularly the ISO 15189: 2007 developed for medical laboratories, are key tools for changing and improving upon every day clinical laboratory practice (Grabber, 2005). The accurate analysis and control of all procedure and processes included in the testing process particularly if effective tools such as FMEA and HAZOP techniques are included, may significantly reduce weakness thus maximizing patient safety. We have learnt that TTP is the unique framework for identifying and reducing error, including initial steps such as patient identification and appropriateness in test requesting and other steps such as communication and interpretation of test results.

The second lesson is that teamwork is the aim of safety, if we wish to improve the appropriateness of test requesting and the reaction to the results. The important of expert support systems, which provide information on diagnosis efficiency and interpretation criteria at the point of care, may play a role, however collaboration among health provider is mandatory for assuring a patient centered approach to reduce error. International projects aiming to develop quality indicators for all steps in the testing process, and to establish related quality specifications may enable clinical laboratories to compare, monitor and improve their performance in every day practice of

clinical scientist. The goals selected by international organization such as the world Alliance for patient safety and the joint commission should be addressing well recognized issue such as communication of laboratory results.

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Ethical Approval

This article does not contain any studies with human participants or animals experiment performed by any of the authors.

Abbreviations

- AACC
  American Association for Clinical Chemistry.
- IOM
  Institute Of Medicine
- TTP
  Total Testing Process
- IQC
  Internal Quantity Control
- EQA
  External Quality Assessment
- PT
  Proficiency Testing
- PPM
  Part Per Million
- δ
  Sigma
- POCT
  Point of Care Testing
- ISO
  International Organization for Standardazation
- TS
  Technical Specification
- FMEA
  Failure Mode and Effect Analysis
- HACCP
  Hazards Analysis and Critical Control Points
- HAZOP
  Hazards and Operability Studies
- WG-LEPS
  Working Group on Laboratory Error and Patients Safety
- IFCC
  International Federation of Clinical Chemistry and Laboratory Medicine

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