EFLM Paper

Pieter Vermeersch*, Glynis Frans, Alexander von Meyer, Seán Costelloe, Giuseppe Lippi and Ana-Maria Simundic

How to meet ISO15189:2012 pre-analytical requirements in clinical laboratories? A consensus document by the EFLM WG-PRE

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Abstract: The International Organization for Standardization (ISO) 15189:2012 standard aims to improve quality in medical laboratories through standardization of all key elements in the total testing process, including the pre-analytical phase. It is hence essential that accreditation bodies, assessing laboratories against ISO15189:2012, pay sufficient attention to auditing pre-analytical activities. However, there are significant differences in how technical auditors interpret the pre-analytical requirements described in ISO15189:2012. In this consensus document, the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for Pre-analytical Phase (WG-PRE) sets out to review pre-analytical requirements contained in ISO15189:2012 and provide guidance for laboratories on how to meet these requirements. The target audience for this consensus document is laboratory professionals who wish to improve the quality of the pre-analytical phase in their laboratory. For each of the ISO requirements described in ISO15189:2012, members of EFLM WG-PRE agreed by consensus on minimal recommendations and best-in-class solutions. The minimal consensus recommendation was defined as the minimal specification which laboratories should implement in their quality management system to adequately address the pre-analytical requirement described in ISO15189:2012. The best-in-class solution describes the current state-of-the-art in fulfilling a particular pre-analytical requirement in ISO15189:2012. We fully acknowledge that not every laboratory has the means to implement these best-in-class solutions, but we hope to challenge laboratories in critically evaluating and improving their current procedures by providing this expanded guidance.

Keywords: accreditation; ISO15189; pre-analytical phase; quality improvement.

Pieter Vermeersch and Glynis Frans contributed equally to this work.

***Corresponding author: Prof. Dr. Pieter Vermeersch**, Clinical Department of Laboratory Medicine, University Hospitals Leuven, Herestraat 49, 3000 Leuven, Belgium; and Department of Cardiovascular Sciences, KU Leuven, Leuven, Belgium, Phone: +003216347091, Fax: +003216347010, E-mail: pieter.vermeersch@uzleuven.be. https://orcid.org/0000-0001-7076-061X
Glynis Frans, Clinical Department of Laboratory Medicine, University Hospitals Leuven, Leuven, Belgium
Alexander von Meyer, Institute of Laboratory Medicine and Microbiology, Munich Municipal Hospital Group, Munich, Germany
Seán Costelloe, Department of Clinical Biochemistry, Cork University Hospital, Cork, Republic of Ireland. https://orcid.org/0000-0002-2464-3735
Giuseppe Lippi, Section of Clinical Biochemistry, University of Verona, Verona, Italy. https://orcid.org/0000-0001-9523-9054
Ana-Maria Simundic, Department of Medical Laboratory Diagnostics, University Hospital Sveti Duh, Zagreb, Croatia; Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb, Croatia. https://orcid.org/0000-0002-2391-5241

Introduction

The total testing process (TTP) is a complex concept in laboratory medicine, originally referred to as the "brain-to-brain" cycle by George Lundberg nearly 50 years ago [1]. The TTP can be summarized as follows: the physician orders the necessary test prescriptions; the patient is identified and prepared for sampling; the samples are collected, transported, identified, stored, and prepared for analysis. All the processes prior to actual analysis, both outside and inside the laboratory, comprise the pre-analytical phase. After analysis, test results are validated, reported, and interpreted by laboratory specialists and requesting physicians, who take further medical decisions based on test results [1].

The overall frequency of errors in laboratory medicine is approximately 0.3%, which remains lower than those of other medical diagnostic disciplines (e.g., histopathology, with an error rate of nearly 5.0%) [2]. The pre-analytical

phase, which is often plagued by a low degree of standardization, is the most vulnerable to errors, so that preventing and/or limiting the impact of pre-analytical errors on patient safety are some of the hardest challenges in laboratory medicine [3]. The frequency of pre-analytical errors typically comprises between 60 and 70% of all laboratory mistakes. In comparison, the analytical and post-analytical phases contribute approximately to 15 and 20% of all errors in the TTP, respectively [4, 5]. Although the pre-analytical phase is mostly performed outside of the laboratory environment, the clinical laboratory has a major responsibility in decreasing vulnerability to these errors. Continuous improvement can be achieved, for example, by systematic error monitoring and registration, application of risk management strategies, development and monitoring of pre-analytical quality indicators, as well as by establishing education and training for healthcare staff [6–8].

In a recent survey disseminated by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for the Pre-analytical Phase (WG-PRE), 1,265 out of 1,405 laboratory specialists (94%) from 37 different countries declared that they monitored pre-analytical errors. However, assessment, documentation and further use of information obtained from errors varied widely among respondents, countries, and even International Organization for Standardization (ISO) 15189:2012-accredited laboratories [9]. A consensus on what to do with these data is clearly lacking. Many responders also stated that whey would be interested in a guideline for measurement and evaluation of pre-analytical variables (n=1,235; 92%) [9].

The ISO15189:2012 standard is aimed to improve quality in medical laboratories by standardization of all key processes, including the pre-analytical phase [10]. However, it is common experience that accreditation bodies for ISO15189:2012 tend to spend only a small amount of time auditing activities occurring before the analytical part of the TTP. There are also significant differences in how technical auditors interpret pre-analytical requirements described in ISO15189:2012. This corresponds to our findings in a recent EFLM WG-PRE survey, where a number of respondents claiming to follow this guideline did not adhere to demands such as continuous improvement activities based on pre-analytical errors or providing pre-analytical instructions to clinicians [9].

The intention of ISO15189:2012 is to guide laboratories to develop a quality management system (QMS) that regulates all steps in the TTP, thus ensuring constant quality of patient care. The ISO15189:2012 describes which procedures and aspects have to be in place, but the authors deliberately chose not to clearly specify in which way or how they should be implemented. Moreover, laboratory professionals often have an obligation to design their QMS in such a way that it also conforms to local regulations regarding accreditation. Further, procedures should be subjected to risk management and continuous improvement based on effectiveness and user experience [11]. Nevertheless, some documents have been published, which provide more elaborate specifications on how to implement ISO15189:2012, including guidance provided by the French accreditation body Comité français d'accréditation (Cofrac) and ISO Technical Specification documents [12, 13].

In this consensus document, the EFLM WG-PRE sets out to review pre-analytical requirements contained in the ISO15189:2012 standard and provide expert guidance for laboratories on how to meet these requirements.

Methods

This document has been produced by the authors, of whom all but one (G.F.) are EFLM WG-PRE members. The first draft of the list of pre-analytical specifications was produced by P.V. and G.F. by thorough screen of ISO15189:2012 for all pre-analytical requirements. The draft was then reviewed and thoroughly discussed by all authors during several face-to-face meetings and conference calls. The final list of pre-analytical requirements described in ISO15189:2012 was then discussed by the entire WG-PRE during two subsequent face-to-face meetings to come to a final consensus of minimal recommendations and best-in-class solutions, which are summarized in this consensus document.

For each ISO requirement described in ISO15189:2012, a specification was agreed by a consensus for what should be considered the minimal recommendation according to EFLM WG-PRE, and what is the best-in-class solution according to EFLM WG-PRE. The minimal consensus recommendation was defined as the minimal specification which laboratories should implement in their QMS in order to adequately address the pre-analytical requirement described in ISO15189:2012. The best-in-class solution describes the current state-of-the-art in fulfilling a particular pre-analytical requirement in ISO15189:2012. We fully acknowledge that not every laboratory has the means to implement these best-in-class solutions but, by providing this expanded guidance, we hope to challenge laboratories in critically evaluating and improving their current procedures.

Evidence for these EFLM WG-PRE recommendations and solutions was graded according to the following scale: (1) directly derived from ISO15189:2012 requirements; (2a) based on existing professional recommendations; (2b) current state-of-the-art technology; and (3) expert opinion. This scaling follows the rationale that ISO15189:2012 should always be followed if any specifications are described in ISO15189:2012. If ISO15189:2012 does not specifically state how a requirement should be met, but there are professional recommendations which do (2a), the laboratory could follow these recommendations (e.g., the joint EFLM-Latin-American Confederation of Clinical Biochemistry (COLABIOCLI) recommendation for venous blood sampling) (2a). In the absence of (1) or (2a), the recommendations were based on current state-of-the-art technologies or expert opinion, which are more subjective and therefore graded. We leave it up to the

readers to investigate whether and how grade 2b and 3 specifications can be applied to their specific laboratory setting.

Results and discussion

The identified elements, with their matching minimal ISO requirement, minimal WG-PRE consensus recommendation, and best-in-class solution are described in three tables: Table 1 for QMS; Table 2 for Blood Collection; and Table 3 for Transport, Reception and Handling. During our review of the ISO15189:2012 standard, we often noted significant lack of clear specifications on how procedures and aspects concerning the pre-analytical phase should be implemented. We noted a particular lack of specifications regarding the pre-analytical phase in terms of continuous improvement (e.g., the type of quality indicators that should be used), validation of sample recipients, transport, and environmental conditions. Some of these issues are discussed in more detail in the following sections.

Pre-analytical quality indicators

ISO15189:2012 requirements and EFLM WG-PRE recommendations concerning pre-analytical quality indicators (QIs) can be found in Table 1. ISO15189:2012 requires laboratories to establish a quality policy with objectives to meet the needs and requirements of all users. To this end, the laboratory shall establish measurable QIs to monitor and evaluate performance throughout critical laboratory aspects, thus including the pre-examination phase. QI monitoring requires definition of the objective, methodology, interpretation, limits, action plan, and time of measurement. QIs are invaluable to confirm that laboratory quality objectives have been met, as well as for measuring efficacy of corrective/preventive actions. In addition, when deterioration of quality of blood collection is noted according to QI analysis, the laboratory must communicate this evidence and provide additional education and training to its users.

ISO15189:2012 suggest some examples of pre-analytical QIs (e.g., unacceptable samples, errors at registration and/or accession, corrected reports), but does not state how they should be monitored and evaluated. As a minimum, we recommend that laboratories should monitor one of the following QIs on yearly basis (e.g., during the management review): number and proportion of misidentification errors, test transcription errors, incorrect sample types, insufficiently filled samples, unsuitable samples, contaminated samples, hemolyzed samples, or clotted samples. We have chosen these QIs because they are included in the priority one category of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Model of Pre-analytical Quality Indicators [8], and because we believe that they are the easiest to implement in most laboratory settings and current-day Laboratory Information Systems (LISs) without requiring significant programming efforts. As a best-in-class solution, we recommend laboratories to monitor pre-analytical QIs in accordance with the framework provided by the IFCC Model, which defines procedures for data collection and provides quality specifications for evaluating laboratory results based on External Quality Assessment (EQA) [8]. We encourage participation in the IFCC EQA scheme for quality indicators [8]. While we acknowledge that monitoring pre-analytical QIs in such a way requires time and resources (e.g., software adaptations, additional EQA registrations), we would like to emphasize that selection of QIs, frequency of evaluation, and their calculation can be adapted to a specific laboratory setting based on risk assessment to identify pre-analytical processes which require higher priority for monitoring (e.g., sample identification or sample collection) [14, 15]. In this context, it should also be emphasized that ISO15189:2012 requires regular re-evaluation of QI methodology to ensure continued appropriateness.

Sample collection

ISO15189:2012 requirements and EFLM WG-PRE recommendations concerning sample collection can be found in Table 2. ISO15189:2012 requires that sample collection needs to be performed by adequately trained personnel, and laboratories should provide and supervise training concerning blood collection for all appointed personnel. In addition, the laboratory should assess competence of each phlebotomist according to established criteria described in the QMS. Reassessment shall take place at regular intervals (see below) and retraining shall occur when necessary, especially when analytical methods and/or instrumentation change. The effectiveness of training programs shall be periodically reviewed, e.g., based on personnel and user feedback. In addition to requirements specified in ISO15189:2012, the authors of this article make a number of additional recommendations. We minimally recommend that the necessary education, training (including scope, duration, competency criteria, and reassessment intervals), skills, experience, and where applicable, certification and licensure for each job title related to venipuncture processes, must be defined in the QMS. Training programs and competence assessments of pre-

Table 1: ISO15189:2012 requirements and corresponding EFLM WG-PRE recommendations/solutions relating to quality management of the pre-examination phase.

ISO paragraph	Question	ISO requirement	Minimal recommendation	Grade	Best-in-class solution	Grade
4.1.2.4 – Quality objectives and planning	How to define quality objectives and quality indicators for pre-examination processes?	The quality objectives shall be measurable and consistent with the quality policy.	Laboratories should at least monitor one of the following quality indicators: number of misidentification errors, test transcription errors, incorrect sample types, insufficiently filled samples, unsuitable samples, contaminated samples, hemolyzed samples, or clotted samples.	2a	Pre-analytical quality indicators are monitored according to framework provided by the IFCC Model of Quality Pre-analytical Indicators. Laboratories should implement all quality indicators that are relevant for their setting based on risk-assessment. Participation in the IFCC External Quality Assessment program is encouraged.	2a
	How frequent should pre-analytical quality objectives/quality indicators be evaluated?	Planning of the quality management systems is carried out to meet the requirements and the quality objectives.	Yearly.	1	Frequency according to the framework provided by the IFCC Model of Quality Pre-analytical Indicators.	2a
4.1.2.5 – Responsibility, authority and interrelationships	Is it required to appoint a person in the laboratory who is responsible for the pre-examination phase? Definition, requirements?	Yes. Appointment of person(s) responsible for each laboratory function and appointment of deputies for key managerial and technical personnel.	A dedicated laboratory staff member should be appointed who is responsible for all pre-examination aspects both within and outside of the central laboratory.	1	A dedicated laboratory medicine specialist should be appointed who is responsible for all pre-examination aspects both within and outside of the central laboratory.	3
4.1.2.6 – Communication processes	Should notifications and problems concerning the pre-analytical phase be communicated to hospital and/or laboratory personnel? How should this be done?	Yes.	Any deterioration of the quality objectives or significant remarks obtained during internal audits shall be communicated and documented.	1	At least half-yearly meetings with all stakeholders to discuss expectations, internal audit results (if performed during that period), quality indicators and non-conformities. This should be done using a well-developed communication plan.	3
4.8 – Resolution of complaints **4.9 – Identification and control of nonconformities**	How should complaints and non-conformities about the pre-examination processes be handled?	Should be handled similar to other complaints, non-conformities, etc. including documentation.	Complaints of the pre-analytical phase should be handled in accordance with the general laboratory policy.	1	–	
4.10 and 4.11 – Corrective and preventive actions	How should corrective and preventive actions concerning pre-examination processes be handled?					

Table 1: (continued)

ISO paragraph	Question	ISO requirement	Minimal recommendation	Grade	Best-in-class solution	Grade
4.12 – Continual improvement	Which aspects of the pre-analytical phase should be discussed during/presented during the management review?	Present evaluation activities, corrective actions and preventive actions for the pre-examination phase.	Preparation of the management review should be handled in accordance with the general laboratory policy.	1	–	
	How should a risk assessment of the pre-analytical phase be performed? Which aspects should be covered?	Not stated.	Risk assessment of the pre-analytical phase should be handled in accordance with the general laboratory policy. The risk assessment identifying the most critical step should be documented.	1	A risk assessment of the pre-analytical steps in the total testing process including identification, patient preparation, sample preparation, sample collection, transport, reception, and sample storage should be performed.	1
4.14.5 – Internal audit	How often should an internal audit evaluate the pre-examination phase?	The pre-examination phase should be evaluated every year (Note 1: the cycle for internal auditing should normally be completed in one year).	Once per year.	1	At least once per year.	1
	Which aspects of the pre-examination phase should be covered in the internal audit?	Not stated.	Pre-analytical phase is part of a general audit.	1	A specific internal audit covering exclusively on all aspects of the pre-examination phase.	3
	How should results of internal audits on the pre-examination phase be communicated to stakeholders?	Not stated.	Any deterioration of the quality objectives or significant remarks obtained during internal audits shall be communicated and documented.	1	At least half-yearly meetings with all stakeholders to discuss expectations, internal audit results (if performed during that period), quality indicators and non-conformities. This should be done using a well-developed communication plan.	3
4.14.6 – Risk management	How should a risk assessment of the pre-analytical phase be performed? Which aspects should be covered?	Not stated.	Risk assessment of the pre-analytical phase should be handled in accordance with the general laboratory policy. The risk assessment identifying the most critical step should be documented.	1	A risk assessment of the pre-analytical steps in the total testing process including identification, patient preparation, sample preparation, sample collection, transport, reception, and sample storage should be performed.	1

Table 1: (continued)

ISO paragraph	Question	ISO requirement	Minimal recommendation	Grade	Best-in-class solution	Grade
4.14.7 – Quality indicators	Which QIs should be monitored and in which manner?	Non-binding examples include number of unacceptable samples, numbers of errors at registration and/or accession, number of corrected reports.	Laboratories should at least monitor one of the following quality indicators: number and proportion of misidentification errors, test transcription errors, incorrect sample types, insufficiently filled samples, unsuitable samples, contaminated samples, hemolyzed samples, or clotted samples.	2a	Pre-analytical quality indicators are monitored according to framework provided by the IFCC Model of Quality Pre-analytical Indicators. Laboratories should implement all quality indicators that are relevant for their setting based on risk-assessment. Participation in the IFCC External Quality Assessment program is encouraged.	2a
	At which frequency should QIs be monitored and analyzed?	Not stated.	Yearly.	1	Frequency according to the framework provided by the IFCC Model of Quality Pre-analytical Indicators [8].	2a
4.15.2 - Management review	No controversy.	Pre-analytical improvements should be included.	Preparation of the management review should be handled in accordance with the general laboratory policy.	1	–	

IFCC, International Federation of Clinical Chemistry and Laboratory Medicine; QI, quality indicator.

analytical procedures should be organized and documented under laboratory supervision. Competence reassessment of all personnel shall take place at least every five years. Finally, the joint EFLM-COLABIOCLI recommendation for venous blood sampling is recommended as best-in-class solution for training and competency assessment [16]. This guideline provides practical guidance on education, practical training, (re-)certification, and auditing of venous blood sampling procedures [16].

The ISO15189:2012 standard requires that facilities where patient sample collection procedures are performed (e.g., phlebotomy) shall enable sample collection to be undertaken in a manner that does not invalidate the results or unfavorably impacts the quality of examinations. As a minimum, we recommend to define specific requirements for dedicated phlebotomy rooms in the QMS. Further guidance on best-in-class solutions concerning the required elements (e.g., chair/bed, hand washing areas, waiting areas, supplies) can be found in the joint EFLM-COLABIOCLI recommendation for venous blood sampling [16].

Although this is not stated in the ISO15189:2012 document, we recommend that the performance of consumables potentially affecting the quality of examinations should be verified before use. As a minimum, the performance of a new type of sample collection system should at least be verified in 20 samples for a subset of tests. The laboratory defines the subset based on risk assessment. We recommend to also perform clinical and technical validation in accordance with EFLM recommendations as a best-in-class solution [17]. This local technical validation should be intended to verify if manufacturer claims about structure, assembly, functionality and safety of blood collection tubes are fulfilled. Preferably, over 240 blood collections should be randomized to both control (n=120) and comparative (n=120) groups, and all relevant technical information should be recorded; e.g., physical defects, vacuum failures, clotting, hemolysis [18]. As alternative and more stringent comparison, collection of two paired tubes from the same patient with the two different systems may be advisable [17]. Whenever reference intervals are verified during implementation of a new sample collection

Table 2: ISO15189:2012 requirements and corresponding EFLM WG-PRE recommendations/solutions relating to blood collection.

ISO paragraph	Question	ISO requirement	Minimal recommendation	Grade	Best-in-class solution	Grade
4.7 – Advisory services	How should information on available laboratory tests and sample requirements be provided to the requesting clinician?	Not stated.	Test catalog (with version control) which contains at least information on available tests, required sample type and volume, stability and transport conditions, and contact details of the laboratory. The laboratory offers advisory services on request for these issues.	1	Searchable (online, app, paper) laboratory guide containing in addition to the minimal recommendation also information on test indication, test utilization and guidelines where relevant. The laboratory offers advisory services on request and organizes educational events organized by the laboratory.	2b
	How should failure of samples not fulfilling acceptance criteria be communicated to the clinic?	Criteria for specimen rejection should be defined in the QMS. A comment shall be added (manually or automatically) to the final report indicating the nature (and the degree) of the problem and the tests for which caution is required when interpreting the results.	As described in ISO15189:2012.	1	The laboratory provides information about the impact on each parameter on the final report. The laboratory shall provide education and training to its customers at their request or whenever deemed due to a deterioration of the quality of the blood collection.	2b
4.14.2 – Periodic review of requests, and suitability of procedures and sample requirements	How often should sample blood collection conditions and test catalog information be reviewed?	Not stated.	Blood collection conditions and test catalog information should be reviewed whenever instruments, methods or sample collections systems change.	1	Blood collection conditions and test catalog information should be reviewed at least every two years and whenever instruments, methods or sample collections systems change.	3
5.1 – Personnel	What are the minimum personnel qualification required for blood venipuncture?	Personnel should be qualified.	The necessary education, training, skills, experience, and where applicable, certification and licensure for each job title related to venipuncture processes must be determined in the QMS. Training programs should be organized and training and competence assessment on all pre-analytical procedures shall be documented.	1	Training and education in line with the EFLM recommendation including regular review of competencies including observational audits [16].	2a

Table 2: (continued)

ISO paragraph	Question	ISO requirement	Minimal recommendation	Grade	Best-in-class solution	Grade
5.1.5 – Training	What should be included in the training program for the pre-examination phase (including sample collection)?	Not stated.	Scope and duration are defined in QMS and training is documented.	1	In line with the EFLM recommendation [16].	2a
5.1.6 – Competence assessment	How do you evaluate competency?	Competence of laboratory staff can be assessed by using any combination of approaches under the same conditions as the general working environment.	Competency criteria are defined in QMS.	1	In line with the EFLM recommendation [16].	2a
	How often should reassessment take place?	Not stated.	An interval for reassessment should be defined in the QMS. Reassessment should take place at least every 5 years.	1	In line with the EFLM recommendation [16].	2a
5.2.5 – Patient sample collection facilities	Are there specific requirements for dedicated phlebotomy rooms?	Not stated.	Specific requirements for dedicated phlebotomy rooms are defined in QMS.	1	In line with the EFLM recommendation [16].	2a
5.3.2 – Reagents and consumables	Do sample collection devices fall under the category of consumables and do they require a documented verification procedure before use?	Not stated.	The performance of a new type of sample collection system should at least be verified in 20 samples for a subset of tests. This subset of tests is defined based on risk assessment.	2a	Clinical and technical validation in accordance with EFLM recommendations [17].	2a
5.4.2 – Information for patients and users	Which information should be available to patients?	Description of the minimal requirements of the documented procedure.	As described in ISO15189:2012.	1	–	
	Which information should be available to users?	Description of the minimal requirements of the documented procedure.	Test catalog (with version control) which contains at least information on available tests, required sample type and volume, stability and transport conditions, and contact details of the laboratory. The laboratory offers advisory services on request for these issues.	1	Searchable (online, app, paper) laboratory guide containing in addition to the minimal recommendation also information on test indication, clinical utility and guidelines where relevant. The laboratory offers advisory services on request and organizes educational events organized by the laboratory.	2b
5.4.3 – Request form information	No controversy.	Description of the minimal requirements of the documented procedure.	As described in ISO15189:2012.	1	–	

Table 2: (continued)

ISO paragraph	Question	ISO requirement	Minimal recommendation	Grade	Best-in-class solution	Grade
5.4.4.2 – Instructions for pre-collection activities 5.4.4.3 – Instructions for collection activities	What is the current standard of care for instructions for pre-collection activities?	Description of the minimal requirements of the documented procedure.	A procedure for sample collection should be available in the QMS.	1	A procedure for sample collection should be available in the QMS which is completely in line with the EFLM recommendation [16]. In addition, the laboratory should guarantee that all procedures are followed by and remain consistent for all phlebotomists, nursing staff, physicians, and other relevant personnel.	2a
5.5.2 – Biological reference intervals or clinical decision values	What are the current guidelines concerning verification of reference values when changing pre-examination procedures?	Not stated.	The performance of a new type of sample collection system should at least be verified in 20 samples for a subset of tests. This subset of tests is defined based on risk assessment.	2a	Verification of the reference interval according to CLSI EP28-A3 [18] or a data-driven approach [19].	2a

QMS, quality management system; EFLM, European Federation of Clinical Chemistry and Laboratory Medicine; CLSI, Clinical & Laboratory Standards Institute.

system, this should be performed according to Clinical & Laboratory Standards Institute (CLSI) standard EP28-A3 [18]. For sample collection systems already in use, where useful data are already available, a data-driven approach can be used as an alternative [19].

Finally, ISO requires that the laboratory shall have documented procedures for appropriate collection and handling of primary samples. As a minimum, we recommend that procedures for sample collection should be available in the QMS and, ideally, these should be in line with current EFLM-COLABIOCLI recommendation for venous blood sampling [16]. When the laboratory changes an examination procedure, ISO requires the laboratory to review the associated reference intervals and clinical decision values, when applicable. As a minimum, we recommend that blood collection conditions and test catalog information should be reviewed whenever instruments, methods or sample collection systems change (e.g., with introduction of a new type of blood tube, see above). For a best-in-class solution, we recommend that blood collection conditions and test catalog information are reviewed at least every year and whenever sample collection procedures are adapted.

Sample transport

ISO15189:2012 requirements and EFLM WG-PRE recommendations concerning sample transport can be found in Table 3. ISO15189:2012 requires laboratories to have a documented procedure for selecting external services and suppliers, to ensure that the quality of the service is guaranteed at all times. In addition, the performance of external suppliers must be monitored and evaluated to ensure that purchased services or items consistently meet required and pre-defined criteria defined in the QMS. These requirements also concern suppliers involved in transportation (on behalf of the laboratory) of patient samples from external venipuncture sites (e.g., general practitioner surgeries) or other laboratories or hospitals. Nevertheless, the ISO15189:2012 document does not state how frequently suppliers should be evaluated and fails to provide specific guidance concerning evaluation criteria. As a minimum recommendation, we propose that criteria pertaining to transport time, transport temperature, or other relevant transport conditions (e.g., acceleration forces for samples conveyed by pneumatic transports systems), as well as traceability and training of personnel and resolution of complaints should be clearly

Table 3: ISO15189:2012 requirements and corresponding EFLM WG-PRE recommendations/solutions relating to sample transport, reception and acceptance.

ISO paragraph	Question	ISO requirement	Minimal recommendation	Grade	Best-in-class solution	Grade
4.6 – External services and supplies	How and in which frequency should sample transport companies be evaluated?	Not stated.	Yearly.	1	At least yearly evaluation of transport times, transport temperature, sample identification, rejection criteria and hemolysis.	3
	Which criteria for evaluation?	Not stated.	Transport times and temperature.	1		3
	Which criteria for selection of transport companies (= external service) should be used?	Criteria should be based on companies' ability to supply external services in accordance with the laboratory's requirements.	Criteria for transport time, transport temperature, and traceability should be defined in the service level agreement including training of personnel and resolution of complaints.	1	Minimal criteria with continuous temperature monitoring during transport with track & trace of samples and their respective transport container during pick-up, travel, and arrival. The specimens must be transported in sturdy, sealed, leak-proof secondary containers/ packaging. If monitoring cannot be performed by the laboratory, the data must be communicated to the laboratory.	2b
4.13 – Control of records	How long should requests for examination and records of receipt been kept?	Reported results shall be retrievable for as long as medically relevant or as required by regulation.	As described in ISO15189:2012.	1	–	
5.1 – Personnel	What are the minimum personnel qualifications required for personnel who are responsible for sample receipt in the laboratory?	Not stated.	Personnel should be formally trained.	1	Minimum requirement and personnel should be subjected to regular reassessment.	1
5.2 – Accommodation and environmental conditions: storage facilities	What are acceptable and minimal accommodation and environmental conditions?	Not stated.	Have documented source for stability.	1	Should be based on own validation data or peer-reviewed original study.	3
	How to monitor temperature?	Not stated.	Periodic measurement of minimum and maximum temperature. Intervals would depend based on risk assessment.	1	Continuous monitoring with online documentation of deviation.	2b
	Acceptable uncertainty and traceability of the temperature measurement?	Not stated.	Annual check of calibration status of temperature probes. A manufacturer's declaration of uncertainty for the temperature probes is available.	1	Check at least twice per year the calibration status of temperature probes. The frequency depends on risk assessment. The manufacturer's claim of uncertainty for the temperature probes has been verified by an accredited laboratory.	3

Table 3: (continued)

ISO paragraph	Question	ISO requirement	Minimal recommendation	Grade	Best-in-class solution	Grade
5.4.5 – Sample transportation	Which elements should be monitored during transport?	PTS.	Analytical bias, hemolysis grades, and G-forces need to be evaluated when implementing a PTS transport system. A possible approach to evaluated analytical bias would be to collect paired samples (one sent by PTS and one by courier) and evaluate the bias between both samples on routine clinical chemistry parameters.	3	Analytical bias, hemolysis grades, and G-forces due to PTS transport should at least be monitored once a year.	3
		Temperature.	Risk assessment to define every transport mode taking at least into account the type of transport, temperature condition, and container type. For each mode monitor min-max T at least once per year during transport.	1	Continuous temperature monitoring during transport with track & trace of samples and their respective transport container during pick-up, travel, and arrival. The specimens must be transported in sturdy, sealed, leak-proof secondary containers/packaging. If monitoring cannot be performed by the laboratory, the data must be communicated to the laboratory.	2b
		Time (collection site to laboratory).	The declared sampling time is known for each sample. Based on a risk assessment, the accuracy of the declared date and time of collection are reviewed regularly. If necessary, corrective action is taken.	1	The exact sampling time is electronically registered during collection.	2b
		Time to centrifugation.	In addition to the declared sampling and laboratory arrival time, an estimation of the time until centrifugation must also be known in the laboratory. Based on risk assessment, the accuracy of this average time until centrifugation must be reviewed regularly. If necessary, corrective action is taken.	2a	The exact sampling time and time of centrifugation is electronically registered.	2b
		Time (laboratory to laboratory).	The date and time of shipping and reception is known for each sample.	1	The exact date and time of shipping and reception is electronically registered.	2b

Table 3: (continued)

ISO paragraph	Question	ISO requirement	Minimal recommendation	Grade	Best-in-class solution	Grade
5.4.6 – Sample reception	Which sample rejection criteria should be in place?	Rejection criteria for problems with identification.	A minimum two and preferably three unique patient identifiers (one of which is the full name of the patient) should be used for patient identification.	2a	Electronic identification of patient and samples at the time of sampling. No further manual data entry steps required during sample reception. In addition, the laboratory has a strategy to monitor, improve and maintain quality of patient identification. The laboratory shall provide education and training to its costumers regarding the importance of patient identification and, at the request of users or whenever deemed due to a deterioration of the quality of the blood collection.	2b
		Rejection criteria for suitability of the sample (e.g., specimen and container type, insufficient sample volume).	Relevant criteria for specimen rejection should be defined in the QMS. Samples not fulfilling these criteria should be rejected unless the sample is clinically critical or irreplaceable and the laboratory chooses to process the sample. It this case, the final report shall indicate the nature of the problem and, where relevant, that caution is required when interpreting the result.	1	The laboratory has an automated system which provides information about the impact of the sample problem on a test by test basis on the final report. The laboratory shall provide education and training to its customers at their request or whenever deemed due to a deterioration of the quality of the blood collection (see also Table 2, ISO paragraph 4.7).	2b
	Which criteria should be evaluated at sample receipt in the laboratory?	Check for factors known to affect performance of the examination.	Relevant criteria for specimen rejection should be defined in the QMS. HIL check should be performed when known to affect performance. Management of samples should be handled according to EFLM recommendations [22].	1/2b	The laboratory has an automated system for detection and reporting of HIL check which provides information about the impact of the sample problem on a test by test basis on the final report. The laboratory shall provide education and training to its customers at their request or whenever deemed due to a deterioration of the quality of the blood collection (see also Table 2, ISO paragraph 4.7).	2b

Table 3: (continued)

ISO paragraph	Question	ISO requirement	Minimal recommendation	Grade	Best-in-class solution	Grade
		Transport temperature and time.	Relevant criteria for specimen rejection should be defined in the QMS. Criteria should be based on manufacturer's recommendations, literature or other sources. If data are not available, the lab should produce their own data. If no continuous monitoring is available, the evaluation should be based on the worst-case scenario (e.g., only min and max T available).	1	Relevant criteria for specimen rejection should be defined in the QMS. Criteria should be based on manufacturer's recommendations, literature or other sources. The laboratory verifies these criteria. If the laboratory cannot verify the criteria or data are not available, the lab should produce their own data. Assessment of the sample acceptance and management with respect to temperature and time should be performed automatically. The laboratory has an automated system which provides information about the impact of the sample problem on a test by test basis on the final report. The laboratory shall provide education and training to its customers at their request or whenever deemed due to a deterioration of the quality of the blood collection.	3
5.4.7 – Pre-examination handling, preparation and storage	How should storage conditions be monitored?	Not stated.	Periodic measurement of minimum and maximum temperature. Intervals would depend based on risk assessment.	1	Continuous monitoring with online documentation of deviation.	2b
	What are acceptable and minimal accommodation and environmental conditions? What are the time limits for routine analysis in the laboratory?	Not stated.	Have documented source for stability.	1	Should be based on own validation data or peer-reviewed original study.	3

QMS, quality management system; HIL, haemolysis-icteria-lipemia; PTS, pneumatic tube system.

defined in the service level agreement. In addition, evaluation of supplier performance should be performed on yearly basis by evaluation of transport time (e.g., time between shipping and reception) and temperature (e.g., min-max temperature data). The accuracy of declared time, temperature, and other relevant transport conditions must be reviewed regularly for each transportation mode based on risk assessment and, when necessary, corrective actions must be undertaken. For best-in-class solution, higher frequency of evaluation (at least yearly) with additional criteria besides transport time and temperature (e.g., sample identification, rejection criteria, and hemolysis) should be performed. Additional possibilities for monitoring include continuous temperature monitoring during transportation, electronic track and trace of samples within their transport container (including collection, pick-up, travel, and arrival), continuous g-force monitoring in pneumatic tube system (PTS) transport and more detailed transport times based on

electronic registration of exact sampling time. We believe that current-day (laboratory) information systems are capable in monitoring these elements. For elements that cannot be monitored by the laboratory itself, data must be monitored by the external supplier and communicated to the laboratory.

Sample reception

ISO15189:2012 requirements and EFLM WG-PRE recommendations concerning sample reception can be found in Table 3. ISO15189:2012 requires that the laboratory QMS defines personnel qualifications including education, training, experience and skills needed for each person involved in the TTP, including sample collection. To ensure that samples received in the laboratory meet acceptance criteria relevant for the requested examination(s), sample reception should only be performed by authorized personnel. As best-in-class solution, we recommend that the appointed staff members should be subject to regular reassessment.

Sample acceptance

The ISO15189:2012 requirements and EFLM WG-PRE recommendations concerning sample acceptance can be found in Table 3. The ISO15189:2012 document requires that rejection criteria for problems with identification, sample suitability, sample integrity, transport time, and temperature are defined in the QMS. If a sample does not meet the acceptance criteria, it should be rejected unless it is clinically critical or irreplaceable. In this case, ISO15189:2012 requires that the final report indicates the nature of the problem and, where relevant, that caution is required when interpreting test result.

As a minimum concerning correct patient identification, we recommend that correct identification of the patient should at least be verified by a minimum of two, preferably three, unique patient identifiers, one of which is the full name of the patient [20]. Each sample should be unequivocally identified and traceable to a unique laboratory request. As best-in-class solution, we recommend that electronic identification of patient and his/her samples occurs at time of blood collection and no further manual data entry steps are needed during sample reception (to avoid any errors). In addition, the laboratory should define in the QMS how it will monitor, improve, and maintain quality of patient identification, preferably by correct use and interpretation of pre-analytical QIs and education of its users (see section on “Pre-analytical quality indicators”).

ISO15189:2012 requires that transport temperature and time are monitored during transport. As a minimum, we recommend that when no continuous temperature monitoring is available during sample transportation, evaluation of sample integrity upon arrival in the laboratory shall be based on the worst-case scenario (e.g., only min and max temperature available). Criteria concerning transport temperature and time should minimally be based on manufacturers’ recommendations or scientific literature. The laboratory QMS must also include time and temperature limits for requesting additional examinations on the same primary sample, and thereby the overall length of storage (e.g., days) that samples will be stored in the laboratory before being discarded. As best-in-class, assessment of sample acceptance with respect to temperature and time should be performed automatically through the LIS, and the laboratory should produce its own stability data concerning storage temperature and time through experimental validation studies.

Concerning sample integrity, we minimally recommend checking for Hemolysis-Icterus-Lipemia (HIL) whenever a requested analysis is known to be affected by these parameters. Afterwards, management of samples checked for HIL should be handled according to EFLM recommendations [21, 22]. The HIL measurement shall be preferably performed using automated systems rather than by visual inspection. For best-in-class solution, the laboratory should implement an automated system integrated with the LIS for detecting, reporting, and interpreting HIL data, which automatically provides information within the final report about the impact of sample problem (negative or positive interference) on a test-by-test basis.

Conclusions

We hope that laboratory professionals will use this document to improve and maintain the quality of the pre-analytical phase in their laboratories. In addition, we also encourage accreditation bodies to implement this document as guidance during their audits, to help harmonizing the auditing of the pre-analytical phase throughout EFLM member societies. We also welcome any feedback from all involved stakeholders to improve future updates of this document.

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