Opinion Paper

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Improving quality in the preanalytical phase through innovation, on behalf of the European Federation for Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for Preanalytical Phase (WG-PRE)

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Abstract: It is now undeniable that laboratory testing is vital for the diagnosis, prognostication and therapeutic monitoring of human disease. Despite the many advances made for achieving a high degree of quality and safety in the analytical part of diagnostic testing, many hurdles in the total testing process remain, especially in the preanalytical phase ranging from test ordering to obtaining and managing the biological specimens. The Working Group for the Preanalytical Phase (WG-PRE) of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) has planned many activities aimed at mitigating the vulnerability of the preanalytical phase, including the organization of three European meetings in the past 7 years. Hence, this collective article follows the previous three opinion papers that were published by the EFLM WG-PRE on the same topic, and brings together the summaries of the presentations that will be given at the 4th EFLM-BD meeting "Improving quality in the preanalytical phase through innovation" in Amsterdam, 24–25 March, 2017.

Keywords: errors; innovation; laboratory medicine; preanalytical variability; quality.

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Introduction

In the era of personalized (precision) medicine, laboratory diagnostics is becoming as vital as ever for diagnosing, assessing therapeutic response and monitoring human pathologies [1, 2]. The assurance of quality throughout the total testing process has always represented a crucial issue in laboratory medicine. Despite the advances that have unquestionably allowed to achieve a much greater degree of quality and safety in diagnostic testing, many hurdles still remain to be overcome, especially in all those activities ranging from test ordering to obtaining and managing the biological specimens [3–5]. In keeping with these issues, the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) has established a specific Working Group for the Preanalytical Phase (WG-PRE), the aims of which are mainly aimed at mitigating the vulnerability of many preanalytical activities, releasing official documents, guidelines and recommendations, as well as providing continuous education for laboratory professionals and other healthcare operators. The WG has already published many documents on the harmonization and/or standardization of preanalytical activities [6–13], and has also been proactive in organizing many educational meetings across Europe. This collective article hence follows the previous three opinion papers that were published by the EFLM WG-PRE on the same topic, in concert with the first [14], second [15] and third [16] join EFLM-BD meetings which were held in Parma, Zagreb and Porto. This article also anticipates and summarizes the concepts expressed in the various lectures of the fourth EFLM-BD meeting "Improving quality in the preanalytical phase through innovation", Amsterdam, 24–25 March, 2017.

How is the EFLM WG-PRE improving the quality of the preanalytical phase in Europe

The EFLM WG-PRE has intensively worked for the last 4 years with a number of key issues. The primary issue has been to disseminate knowledge about the importance of preanalytical factors to relevant persons within the laboratory milieu all across Europe. This has been achieved through the three previous EFLM-BD European Conferences on the Preanalytical Phase and by publication of opinion papers and a number of study results – an effort that hopefully will continue. The second issue has been to identify key areas, where either knowledge was missing or where the existing knowledge needed clarification. This led to a more focused effort within a number of topics, namely fasting, patient and sample identification, tube validation, order of draw and venous blood sampling. Clarification studies, recommendations or opinion papers have been published about all these topics, with the primary goal to cover the preanalytical area with EFLM guidelines, enabling national societies as well as local laboratory entrepreneurs to improve the conditions within the preanalytical area.

What is the hospital point of view about laboratory innovations

Many ongoing policies contemplating substantial changes in healthcare systems have a deep impact on the organization and structure of laboratories, as well as on and the relationship between laboratory professionals, physicians and patients.

There is a mounting debate between healthcare administrators, who increasingly consider clinical laboratory as a commodity, and laboratory professionals, who instead forcefully defend the role of laboratory as a facility providing high value in terms of the ratio between cost and outcomes [17]. Although the vast majority of general costs of the total testing process is attributable to extra-analytical issues, the various aspects of preanalytical phase, as well as their actual impact on quality and interpretation of test results is usually underestimated in this debate. Centralization of laboratories is universally driven by healthcare organizations to cut down costs [18]. Laboratory activity is characterized by high throughput and short turnaround time (TAT), but the transportation of biological materials remains a real but mostly neglected issue [19]. Hence, the transportation modalities should be clearly specified and standardized, also pertaining to those tests usually performed in specialized laboratories (e.g. metabolomics, micro RNAs, liquid biopsy), as well as prenatal screening of congenital diseases (e.g. cell-free fetal DNA).

Soon the European Union (EU) is expected to release a new set of regulations for medical devices, which will then be implemented for the next 2 years. Hence, the role of laboratories in evaluating medical devices will be strongly emphasized, also entailing the generation of documents supporting the quality of devices and proposing supplies of different devices. This practice is essential at a local level, but the role of preanalytical phase experts will also be important for defining and

evaluating the general characteristics of devices and/or procedures [10]. Notably, the use of health technology assessment (HTA) for evaluating new technologies and devices is universally appreciated by national/regional healthcare systems, but will increasingly be used in the field of in vitro diagnostic testing [20]. A machine learning approach using computer-assisted programs may also emerge as a breakthrough for evaluating and interpreting laboratory data, especially for validating reference ranges in association with many other individual and demographical characteristics.

Innovations: from the point of view of the medical company

Innovation by medical companies is more than just good product design. It starts by understanding end user needs and expectations, through design, development and manufacturing phases, with innovation in how the product is justified to hospital management and in its successful implementation. The research and development strategies such as global product development process (GPDS), design for six sigma (DFSS) and six sigma manufacturing are crucial to this success [21]. In order to understand needs, interviews are conducted, questionnaires implemented, processes observed and partnering with key stakeholders completed throughout the design and implementation process. With the design of a new separator technology Becton Dickinson (BD) (Becton Dickinson, Franklin Lakes, NJ, USA), interviewed hundreds of end users and a clear message was the need for both quality and efficiency benefits. Initial prototypes were tested in 'real life' hospital environments, to understand how the design worked which influenced the final design.

Understanding patient needs and product usage has led to new designs that are both more comfortable for the patient and easier to use, resulting in improved patient satisfaction, safety for the end user and sample quality (e.g. ultra-thin wall needle technology, enabling smaller gauges to be used, improving patient comfort without impacting the sample quality) [22, 23].

The end user has to be able to justify the product to their management, through demonstrating the functional performance and the financial benefits of the products. In the case of the BD Barricor, through its eValidate program Becton Dickinson can provide a customized validation formulary. Functional and financial benefits are demonstrated through performance studies and budget impact models. These are all part of expected service innovations that go hand in hand with product innovation. This delivery of both product and service innovation enables the successful implementation of new products that benefit the laboratory, the patient, the nursing staff and the hospital management.

Preanalytical resource center at Haukeland University Hospital

To deal with challenges within the preanalytical field, the Laboratory of Clinical Biochemistry at Haukeland University Hospital has established a preanalytical resource center, including also other laboratories in the laboratory clinic such as sections for microbiology, endocrinology, pathology, medical genetics and molecular medicine, immunology and transfusion medicine. The center consists of biomedical laboratory scientists, scientists with PhD degrees and a professor, all with several years of experience within laboratory practice and preanalytical research. The professional development, research, instruction and education within the preanalytical field are the main focus of the center, aimed at gathering expertise, making visible and improving the competence within the preanalytical field; stimulating preanalytical research; supervising Master's and PhD students within preanalytical research; offering guidance to public health workers and researchers; and presenting news and information at the preanalytical resource center web page.

"Blodprøvetaking i praksis" (Phlebotomy in practice) [24], which was written and published by biomedical laboratory scientists working in the local laboratory. One scientist graduated for the PhD grade "Estimation of Preanalytical Uncertainty in Clinical Chemistry" [25]. Evidence-based procedures for venous and capillary phlebotomy, and accurate patient identification have been published at Helsebiblioteket (Health library) [26]. Preanalytical sample handling instructions for biochemical components are given in the database "analyseoversikten.no".

The center is arranging internal lessons, gives lectures and participates at conferences aimed at increasing the knowledge about preanalytical variables. We are also supervising Master's degree students within preanalytical research. We are also involved in the recently established Biobank Haukeland. Research is an ongoing enterprise for estimating preanalytical uncertainty, patient safety and identification.

Innovations within the laboratory

Many laboratories are currently considering the installation of total laboratory automation (TLA) systems for routine clinical chemistry and laboratory hematology. Advantages of TLA include cost reduction and improved TAT. Since 2010 a TLA system was installed at University Hospitals Leuven (Belgium) for routine chemistry, immunochemistry, infectious serology, hematology, coagulation and hemoglobin A_{1c} (HbA_{1c}). The track offers the possibility for bulk input, volume detection, aliquoter and storage. To further improve the preanalytical workflow, TLA was combined with a number of additional measures including electronic order entry on the wards, use of plasma instead of serum and partial automation of our workflow for therapeutic drug monitoring and 25-OH-vitamin D.

Liquid chromatography tandem mass spectrometry (LC-MSMS), which has been used in specialized laboratories for decades, has become increasingly popular in clinical laboratories in recent years. This is mainly due to the high sensitivity and specificity of this technology. The main applications in routine clinical practice include therapeutic drug monitoring, clinical toxicology and hormonology. Nevertheless, integration in a routine workflow, and hence application in routine laboratories, is still hampered by laborious and difficult-to-automate sample pretreatment protocols. This is particularly true for whole blood analysis. The LC-MSMS analyses are therefore often performed by dedicated laboratory technicians and their incorporation into routine workflow remains a challenge.

Recently, the preanalytical sample pretreatment has been partially automated in the laboratory of University Hospitals Leuven, also incorporating LC-MSMS analysis for tacrolimus, cyclosporin, everolimus and sirolimus and 25-OH-vitamin D into the routine workflow. These LC-MSMS analyses can be performed by the same laboratory technicians in charge of the routine clinical chemistry platform.

How using technology can improve phlebotomy and create better sample quality

The North Bristol NHS Trust's aim is to provide "exceptional healthcare personally delivered", which the trust monitors through patient satisfaction surveys. As part of this ethos to meet the needs of patients, and strive to provide exceptional healthcare, the combined Blood Sciences has been innovative in how it manages and improves the quality of phlebotomy services it provides to the Trust. Key to improving the quality of the service is monitoring and continuous improvement of the phlebotomy process, to this end each phlebotomy staff member has a "P Number", which is recorded with each sample collected. If preanalytical issues are identified, the staff member responsible can be contacted, corrective action taken and focused education and training provided when needed.

The phlebotomy service has worked since 2012 to review and implement blood collection devices that ensures sample quality and enhances patient care. Two safety devices with integrated "flash" to indicate the correct insertion into the vein, the BD Eclipse™ Signal™ blood collection needle (Becton Dickinson) and BD Vacutainer® The Push Button Blood Collection set (Becton Dickinson) was trialed and implemented, with training to ensure that the correct device was used for venous access in different scenarios.

Both devices increased healthcare worker safety with 71% reduction in needlestick injuries recorded for blood collection set [27]. Phlebotomy staff liked the ergonomic design and the safety improvements in both products, and felt that the product design matched the needs of phlebotomy team. There have updates to the devices such as the BD UltraTouch™ technology on the blood collection set which have increased the internal diameter of the needle lumen, whilst maintaining the same external diameter [28]. These changes increased the flow rate of blood into the sample tubes, and decreased the penetration force, which have resulted in positive patient feedback during their use.

Managing laboratory demand strategies: some actual examples of their usefulness

Clinical laboratory plays a dominant role in the overall health care process, as diagnostic information is involved in as many as 70% of clinical decisions. The multi-step laboratory process begins when the clinicians choose the tests and ends when interpreting laboratory reports. Evidence was found that under-requesting diagnostic tests may result in failed disease prevention, missed diagnosis and improper disorder monitoring. On the other hand, over-requesting tests generates high costs and may lead to further unnecessary testing and significant adverse effects [29]. The clinical laboratory is susceptible to turning into

a solely data-vending industry, and the clinical laboratory professional is at risk of not considering knowledge delivery instead of data. The results of some tests may not be useful in certain diagnoses but could hide valuable information. Overall, inappropriately requesting laboratory tests not only jeopardizes the clinical decision making and patient safety, but also dissipates valuable health system resources.

The Appropriate Utilization of Laboratory Tests Group (REDCONLAB) was created to build a network of shared knowledge among Spanish clinical laboratories, with the aim of providing health services of the highest quality in the context of management excellence. Through the study of regional differences with the use of key performance indicators (KPIs), a globally high variability inappropriateness of test requests could be detected. A series of automatic strategies were designed and according to scientific evidence, in consensus with clinicians and based on laboratory information systems (LISs) and patient data bases (PDBs). Specific interventions aimed to decrease the number of uric acid and transferrin tests were designed and implemented in primary care settings, which generated a significant decrease of allopurinol prescription by general practitioners and were also associated with considerable savings. To deal with the low number of requests of both calcium and HbA_{1c}, additional strategies were designed for detecting asymptomatic hyperparathyroidism and occult diabetes, yielding to a mean cost per patient lower than €100, so increasing laboratory visibility and maximizing the benefits for patients and society [30–32].

Targeted thyroid testing in acute illness – achieving success through audit and teaching

Thyroid test results in acutely ill patients are often abnormal, discordant and confusing. They are also mostly ignored by physicians who order them, and not repeated or followed up. Hence, it is plausible that they may not enhance patient outcomes. Despite the above, there is evidence that thyroid testing is on the increase, in an effort to diagnose subtle thyroid abnormalities which benefit from intervention, and because symptoms of thyroid disease are very non-specific. These thyroid abnormalities, part of what is now called the non-thyroidal illness syndrome (NTIS), are known to affect up to 40%–70% of acutely ill patients, and are known to occur in non-critically ill patients as well. The mechanisms of NTIS are multiple and complicated, and are now becoming clearer. Hitherto, there has been no convincing evidence of a benefit to intervention with thyroid hormone. The difficulty in interpreting discordant thyroid results, the lack of clarity about the benefits of intervention, and potential cost savings, favor a restricted thyroid testing policy. Amongst the methods of reducing thyroid test requests in these circumstances, altering requestor behavior is an attractive option. In this regard, audits of local practice, the issue of guidelines (reducing thyroid tests from 53.8% to 21.7% in acutely ill subjects; $p = 0.01$), and education of healthcare professionals (reducing thyroid tests requested per patient from 0.32 before intervention vs. 0.08 post intervention; $p < 0.001$) have been successful, and have significantly reduced thyroid testing where they have been tried [33, 34]. We currently recommend that thyroid tests should be restricted during acute admissions to only those with (a) known thyroid disease, (b) clinical features and risk factors for thyroid disease, (c) the use of drugs potentially affecting thyroid function, and (d) the presence of unexplained tachydysrhythmias.

Diagnostic pathways – when? how? benefits

Effective test ordering, based on guidelines rather than "gut feelings", is a serious issue in the pre-analytical phase – especially in the context of diagnosis related group (DRG)-based reimbursement in hospitals. In 2006, the German Association for Clinical Chemistry and Laboratory Medicine started an initiative aiming to define specific rules for implementation of standardized diagnostic pathways [35]. In 2011, the task force published a widely recognized handbook, which is also available in English [36]. Meanwhile, the task force represents four German-speaking countries (Germany, Austria, Switzerland and Liechtenstein).

Diagnostic pathways are an essential subset of clinical pathways, combining the principle of stepwise reflex testing with a management concept that helps to fulfill medical needs with economic efficacy. The computational basis "if…then…else" rules can easily be visualized as decision trees. From a laboratory perspective, diagnostic pathways represent "smart" test profiles, which – in contrast to inflexible profiles – are not necessarily worked off completely, but just to the point where a diagnostic decision can be made. The handbook includes over 80 such decision trees, which have been worked out jointly by laboratory and clinical experts and are based on published guidelines, whenever possible. The standardized format

facilitates the implementation of the underlying rules in electronic order entry and laboratory information systems.

The benefits of the diagnostic pathway concept are many. Decision trees make the optimal diagnostic pathway transparent, thus improving the mutual understanding between laboratory and clinicians. Automatic ordering of smart profiles saves time, avoids errors at clinical sites and provides the laboratory with a tentative diagnosis or clinical question. Guideline-based ordering improves outcomes and saves money by making sure that no essential tests are missed, while unnecessary requests are avoided. Stepwise testing reduces the number of false positive results, especially when decision limits are based on contemporary statistical algorithms.

Drivers for and examples of demand management in the UK

Most hospitals in the UK National Healthcare System (NHS) operate with a financial deficit, so leading to pressure from various sources for saving money. Laboratories are being driven to do this by commissioners, clinicians, professional bodies as well as from within the laboratory. One strategy for laboratories to save money is reducing the number of tests performed, the other entails reducing the staff. This can be done by reducing the number of inappropriate laboratory investigations, i.e. by managing demand. Nevertheless, the profession must remain patient-centered and demand management should not be about just ensuring that unnecessary tests are requested, but also ensuring that the physicians get the right tests, at the right time, done in the right way and in a reasonable time. Demand management will thus increase some test numbers and decrease others, so that the better strategy may be tailored to target appropriate test requesting and not managing demand.

Fryer et al. [37] suggested a list of 27 recommendations for demand management. The first few of these focus upon establishing benchmarks. There have been a number of UK initiatives to perform this function, including the NHS Atlas of Variation and Keele University Bechmarking Project. This resource highlighted the huge variation existing in requesting practices between different users, which appeared mostly attributable to clinical practice and not variation in patient populations [38]. There are various tools that can be used to ensure appropriateness of testing, and all these require collaboration between the laboratory and its users. Establishing agreed clinical condition specific profiles is one mechanism to ensure that the right tests are performed to properly investigate the clinical query. By adding automated cascade testing to this, laboratories can ensure that only the right tests are performed. Minimum retest intervals can also be used to ensure that tests are only repeated after a clinically relevant timeframe and not before [39]. Finally, education is also a key determinant to ensuring that only appropriate testing is performed [40].

"Choosing Wisely": a US initiative to reduce wasteful practices in medicine

The American Board of Internal Medicine Foundation, in concert with nine other US medical specialty boards, introduced the "Choosing Wisely" campaign in April of 2012 to improve medical decision making by physicians and patients [41]. As the choice to order a laboratory test is the first step in the so-called "brain to brain" loop, this initiative can be viewed as a national effort to improve the very earliest part of the preanalytical phase. Over the past 5 years, the initiative has grown with hundreds of recommendations from over 70 medical societies, accessible on a website [42], which also hosts patient-directed recommendations in partnership with the US non-profit organization Consumer Reports. Unlike guidance from other medical organizations, the items in Choosing Wisely lists are usually directives aimed not to avoid doing something, rather than recommendations to take any specific action. Recommendations dealing with laboratory testing include the Society for Hospital Medicine and the Critical Care Societies Collaborative both individually discouraging daily laboratory testing on inpatients, the American Academy of Allergy, Asthma and Immunology exhortation to avoid indiscriminate immunoglobulin E (IgE) batteries evaluating allergy, and the American Society for Clinical Pathology recommendations to use troponin instead of creatine kinase MB (CK-MB) and not ordering expanded lipid panels, among other recommendations. The Choosing Wisely initiative has now moved towards focusing on interventions that implement the recommendations, with numerous success stories (Choosing Wisely "Champions") linked on their website. While the initiative has not gone without criticism, i.e. not all recommendations have been developed with standardized methodology or undisputed evidence [43], and other recommendations are perceived as difficult to implement [44], the initiative still represents an important attempt to reduce overutilization of medical interventions, including

laboratory testing, that are not expected to be beneficial for the patients.

Challenges of point-of-care testing in the intensive care unit

Critically ill patients in intensive care units (ICUs) are treated for life-threatening disease and intensivists must deal with sudden evolution of the clinical course, so undertaking prompt and appropriate clinical decisions. Rapid biological assessment is a keystone for decision-making process. Thus, the long TAT from blood sampling withdrawal to the test result (mainly attributable to issues related to sample shipping) must be shortened to deal with emergency situations. The use of point-of-care testing (POCT) offers a real advantage in the management of ICU patients. It substantially reduces the TAT for delivering results and provides immediate answers to physician interrogations. It was actually demonstrated that a blood gas analyzer located in an ICU strongly contributes to rapid medical decision-making process, including ventilator setting adjustment along with red blood cell transfusions or emergency treatment of dyskalemia [45]. The "therapeutic" TAT (i.e. the time between ordering a test and interpretation of its results to undertake a final decision) was reduced to 15 min with the POCT, compared to 2 h with the central laboratory [45]. Therefore, an increasing number of ICUs have included POCT devices in their technical facilities. Many tests such as bicarbonate, pH, partial pressure of carbon dioxide (pCO2), partial pressure of oxygen (pO2), sodium, potassium, ionized calcium, hematocrit, glucose, lactate, creatinine, chlorine are currently measured at bedside. Markers of organ failure such as cardiac troponin, brain natriuretic peptide, neutrophil gelatinase-associated lipocalin (NGAL) are also increasingly used. ICUs have access to advanced equipment and will probably absorb further innovating POCT technologies in the future. For instance, smartphone-based diagnostic approaches will probably usher in a new chapter in POCT. Although these technological innovations are highly exciting for physicians, POCT analyses are performed by non-laboratory staff, in diverse clinical contexts in which the POCT users have varying levels of experience with the device. The preanalytical phase, performed outside the direct supervision of laboratory professionals, could be an important reason for variability of POCT performance. Studies on reliability of POCT in ICU have provided controversial results, but these investigations were mainly focused on the analyzer rather than on the preanalytical phase. When integrating the global process of POCT, from the bedside to final result, it was clearly demonstrated that an identical analyzer could provide various quality of results according to the local constraint of the ICUs [46]. Although internal quality programs are implemented by POCT suppliers, these systems cannot overcome all the issues generated during the preanalytical phase. Interestingly, the underperformance of POCT can be significantly improved, so providing reliable results by a tight collaboration between users (ICU staff) and providers (laboratory staff). It is now possible to bring laboratory tests closer to the patient, but it is imperative to monitor their reliability in the exact condition of use.

POCT innovations from a labatory point of view

The implementation of POCT in an emergency department (ED) setting has been suggested as a means to increase timely discharge rates, shorten length of stay and increase patient throughput.

An increase in waiting and processing time, a lack of beds, capacity in the ED, a general perception of being rushed by emergency physicians and staff, increased ambulance diversions and increased frequency of patients leaving the ED without being seen, are all signals that the ED is overcrowding.

The use of history electrocardiogram age risk factors troponin (Heart) score may help mitigating this overcrowding situation by reducing the number of patients in the ED. The triage of patients with chest pain usually occurs in the hospital emergency room. It has been shown that the HEART score offers a simple and quick risk-stratification tool for these patients. Results of the FamouS Triage demonstrate the feasibility of a pre-hospital chest pain triage in the ambulance by paramedics [47].

Innovations regarding glucose measurements are focused on stabilizing glucose in tubes, interstitial continuous glucose measurement (CGM), intravenous CGM and non-invasive glucose measurements. CGM may suffer from a lack of time in respect to venous blood glucose levels. CGM can provide additional information regarding both direction and rapidity of change of glucose values. As such, it can be of additional value to patients for preventing derangements of glucose values. Non-invasive glucose measurements are in development, and may also suffer from this lack of time. Sophisticated software can be helpful for timely warning of patients. A good laboratory verification protocol for CGM is currently lacking. Its

development may thus help to test combinations of conditions that only occasionally will be observed in patients and may therefore not be present during patient evaluation studies. POCT is also applied for home-care of heart-failure patients and may help to improve medication adjustments.

Innovation in the preanalytical phase of POCT testing

POCT, most frequently performed in the ED, ICUs and operation rooms, provides rapid diagnostic information about patient status, enabling faster clinical decision-making, intervention and increased patient throughput, but is also increasingly used in extra-hospital settings such as pharmacies and markets, for auto-screening and auto-diagnosis [48]. The POC tests are typically performed with venous, arterial or capillary whole blood samples, depending on the specified analyte and required patient care. While POCT offers quicker test turnaround and ease of use, the benefits may be offset by less analytical sensitivity/precision and higher risk of interferences [49]. Although analytical issues are very frequent, preanalytical errors account for up to 32% of POC errors. This may be underestimated, as preanalytical errors may go undetected due to lack of user knowledge and limited systems for identifying errors [50].

Innovation by medical companies is more than just good product design. It starts by understanding user needs and expectations. To understand these needs, interviews are conducted, questionnaires implemented and customer processes observed. Recent research has highlighted important issues about the current acute care POC tests, as conveyed by clinicians. Minimizing errors due to preanalytical variables has been identified as an important unmet need. Other issues included poor sample quality (hemolysis, micro-clots, air bubbles), sample handling challenges, inefficient workflow due to complex sample collection, and risk of healthcare worker exposure to bloodborne pathogens. Unlike core labatory processes, sample collection and management are not standard, with facilities implementing unique solutions. These processes can lead to safety concerns from unnecessary needle and blood exposure. Currently, frequent training, monitoring and competency assessment of the diverse users who collect POC samples (nurses, phlebotomists, respiratory therapists and other health professionals) are the only risk mitigation tools available to manage POC preanalytical variability.

Once understood, key unmet customer needs are utilized to design and develop devices that address this envisioned future in POCT, so helping to improve healthcare worker and patient safety and optimizing outcomes for patients and hospital.

Pre-analytical EQAS program for POCT users

A substantial difference exists between pre-analytical external quality assessment scheme (EQAS) program for POCT and for central laboratory users [51]. Concerning POCT users, the EQA organizers are communicating directly with the users of tests and their co-workers. It is therefore important that this category of health personal find the EQA program useful and to the benefit of their patients [52]. The Norwegian Quality Improvement of Laboratory Examinations (Noklus), for example, offers different kinds of pre-analytical programs for POCT users: (1) Pre-pre examinations program about what to test to request and what to analyze in specific clinical situations. This is often performed through case histories, circulated to general practitioners (GPs) and clinicians in nursing homes. Such programs are often combined with a post-examination program about test interpretation. Typical examples are case histories about the use of urine strips, C-reactive protein (CRP) and the international normalized ratio (INR). (2) Pre-examination surveys concerning what procedures GP-offices or nursing homes have for exampling concerning handling of capillary and venous samples and patient identifications. Feedback is given and consists of guidelines and recommendations for specific topics. E-learning programs are developed both for clinicians and co-workers.

EFLM WG-PRE project: European recommendation for venous blood sampling

Venous blood sampling is the most common invasive procedure in health care, available worldwide. Furthermore, venous blood sampling is the most common source of preanalytical variability, which may not only jeopardize sample quality but also put patient safety at risk. Although commonly considered as a simple procedure, the truth is that skilled and educated personnel with a good understanding of the procedure and associated

risks are of the utmost importance in order to minimizing the risk for compromising the quality of the sample and ensuring patient safety during the venous blood sampling procedure [53]. Unfortunately, many European countries do not have their own national guidelines for venous blood sampling. Moreover, there is a large heterogeneity of the staff which currently performs venous blood sampling in Europe in terms of their background education, life-long learning opportunities, medical education, competence and skills [54]. Education about preanalytical phase is not available even at a large proportion of university level curricula in biomedicine and original studies have demonstrated that students in biomedicine are not well educated about the various sources of preanalytical variability [55]. Obviously, there is a room for improvement and harmonization of this important preanalytical step is necessary. The EFLM WG-PRE has this issue high on its agenda and has therefore recently initiated a project with the aim to develop joint consensus recommendation for venous blood sampling practices in Europe. This document has been developed in close collaboration of representatives from over 1/3 of all EFLM national societies as well as with representatives from the association of nurses, phlebotomists and IVD partners and is now in its final stage. Focus and guidance on the implementation of the guidelines is what makes the added value of this document in comparison with already existing guidelines and recommendations. Moreover, the EFLM recommendation is accompanied by some useful tools which are developed by the EFLM WG-PRE and will be made freely available for all EFLM national societies and other interested parties from the EFLM website. The EFLM WG-PRE is hoping that this document will be endorsed by all EFLM national societies. Only through such universal acceptance and implementation, can true harmonization of venous blood sampling and patient safety improvement across Europe be achieved.

Obviously, improving preanalytical quality is a challenging enterprise, requiring major effort throughout the various phases of this process and implementation of various interventions, such as education, regular monitoring and audits. Among the various interventions, broadening EQA schemes to blood collection and other extra-analytical activities should be regarded as a valuable perspective. Such initiatives are not only educational but can also aid in identifying critical steps and room for improvement. One such initiative was recently described in a study summarizing results from six rounds of preanalytical EQA during 2014–2016 in 175 Croatian laboratories, which showed that major critical spots during phlebotomy in Croatia were the lack of availability of safe-sharp needles, disposable tourniquets and glucose inhibitor tubes. The data may obviously differ from country to country, pointing to the need for more engagement of national professional associations in this area to assess the local specificities and requirements [56].

Presentation of the Austrian pilot study on venous blood sampling

The WG-PRE is currently working to drafting a consensus guideline for venous blood collection and sample handling, including an adaptable PowerPoint (PPT) presentation, reflecting the contents of the guideline, a test to examine the knowledge after training as well as an observational checklist to be able to see if the trainees are using their newly gained knowledge correctly in practice. Whereas the observational checklist has already been successfully piloted in one laboratory in Odense (Denmark) [57], here we wish to present the results of the pilot project on venous blood sampling in one Austrian hospital.

A pilot study was recently undertaken involving the pediatric wards of the University Hospital of Salzburg (Austria) to evaluate practicability in a real life health care setting, where phlebotomy tasks were shifted from physicians to the nursing staff. The PPT presentation including the mentioned knowledge test which was transformed into an e-learning module with a single-user login. All 240 pediatric nurses were advised to complete this module and at least 70% of questions had to be answered correctly in the mandatory knowledge test. Practical training using demo arms was also carried out under the supervision of experienced nurses. Practical skills were randomly monitored by using the mentioned observational sheets to evaluate their practical usefulness. In a study performed on other wards of the same hospital, preanalytical education was found to be effective for improving sample quality even if the phlebotomy task was shifted from few experienced health care workers to inexperienced staff [58]. To gain phlebotomy skills, and subsequently improving sample quality, experience time is needed. Unfortunately, it seems too early to evaluate respective data from our pediatric wards at this point in time. As our pilot study was aimed to evaluate the upcoming consensus guidelines and the accompanied documents, we can however conclude that these may be regarded as valuable tools, which were very well accepted by our nursing staff. They are adaptable to fit local health care settings and regulations and very easy to implement. Given the precondition of the hospital management backing such an educational

project, we found the guidelines and the tools a very practical solution to implement standardized venous blood collection and sample handling even in large collectives.

Managing the quality of blood sampling through education

Improved knowledge and awareness of clinical guidelines reduces mistakes in health care. The application of clinical guidelines, as well as the way they are implemented, are impacted by several issues [59]. An intensive effort to implement and sustain adherence to venous blood sampling guidelines among phlebotomists has been carried out between 2009 and 2016 in Västerbotten County Council, Sweden. In 2009, staff attended a compulsory education comprising of 2-h oral lecture and a knowledge test on venous blood sampling guidelines practices. Evaluation of education demonstrated improvements in self-reported practices, such as patient identification and test tube labeling, but blood sample quality monitored as sample hemolysis only showed minor differences.

Web-based programs can be appropriate for large organizations, are cheap and give flexible opportunities as they are accessible for phlebotomists in rural areas [60]. Therefore, in 2013 we replaced the traditional education with a web-based program developed in cooperation with media educators, phlebotomists and university lecturers. The final web-based program includes appropriate monitoring and feedback mechanisms, contains instructive movies, interactive assignments along with clickable explanatory text. It also highlights high risk steps such as patient identification and test tube labeling to ensure patient safety [61].

We then investigated whether the web-based program was effective to improve venous blood specimen collection practices compared to the traditional educational program. Phlebotomists (n = 460 in 2007; n = 995 in 2013; n = 459 in 2016) self-reported adherence to venous sampling guidelines was collected through a validated questionnaire. We also collected user experiences regarding e-learning to assess its usefulness and to perform necessary corrective measures. The questionnaires was analyzed using statistics and content analysis. Preliminary results show that the adherence to venous blood sampling guideline practices was improved with respect to identification procedures and test tube labeling, and that phlebotomists perceived that the web-based program allowed direct feed-back, motivated reflection and was easy to navigate.

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