Viviane Van Hoof*, Suzanne Bench, Antonio Buño Soto, Peter P. Luppa, Anthony Malpass, Ulf Martin Schilling, Kevin D. Rooney, Adam Stretton and Andrei N. Tintu

Failure Mode and Effects Analysis (FMEA) at the preanalytical phase for POCT blood gas analysis: proposal for a shared proactive risk analysis model

Abstract

Objectives: Proposal of a risk analysis model to diminish negative impact on patient care by preanalytical errors in blood gas analysis (BGA).

Methods: Here we designed a Failure Mode and Effects Analysis (FMEA) risk assessment template for BGA, based on literature references and expertise of an international team of laboratory and clinical health care professionals.

Results: The FMEA identifies pre-analytical process steps, errors that may occur whilst performing BGA (potential failure mode), possible consequences (potential failure effect) and preventive/corrective actions (current controls). Probability of failure occurrence (OCC), severity of failure (SEV) and probability of failure detection (DET) are scored per potential failure mode. OCC and DET depend on test setting and patient population e.g., they differ in primary community health centres as compared to secondary community hospitals and third line university or specialized hospitals. OCC and DET also differ between stand-alone and networked instruments, manual and automated patient identification, and whether results are automatically transmitted to the patient's electronic health record. The risk priority number (RPN = SEV × OCC × DET) can be applied to determine the sequence in which risks are addressed. RPN can be recalculated after implementing changes to decrease OCC and/or increase DET. Key performance indicators are also proposed to evaluate changes.

Conclusions: This FMEA model will help health care professionals manage and minimize the risk of preanalytical errors in BGA.

Keywords: blood gas analysis (BGA); failure mode and effects analysis (FMEA); patient safety; point-of-care testing (POCT); preanalytical error; risk management.

Introduction

Key reason for using point-of-care testing (POCT) is the rapid availability of results, allowing prompt clinical decision-making without the need to send samples to a central laboratory. For safe, effective, and person-centred care, it is imperative that POCT results are absolutely accurate and reliable. POCT technology is already well established in emergency departments (ED) and intensive care units (ICU). Although the use of this type of testing generally does not require specific technical laboratory skills, POCT provision and use should be guided by a clinical laboratory and performed by trained and certified personnel only [1].

The three phases of clinical laboratory testing: pre-analytical, analytical and post-analytical also apply to POCT. This article focuses on the pre-analytical phase, known to be responsible for up to 62% of all errors in laboratory medicine [2, 3]. Some preanalytical risks apply to all laboratory tests, including POCT, e.g., wrong or absent sample identification, while other risks are specific for the central laboratory test or for the POCT under consideration.

POCT blood gas analysis (BGA) was chosen as subject for this risk analysis, as it is one of the most complex POCTs, combining the measurement of blood gases,

*Corresponding author: Viviane Van Hoof, MD, PhD, Prof. Em. Medical Biochemistry, Faculty of Medicine and Health Sciences, University of Antwerp, Campus Drie Eiken, Universiteitsplein 1, 2610 Wilrijk, Belgium, E-mail: viv.van.hoof@outlook.com

Suzanne Bench, Guys and St Thomas NHS Foundation Trust, London, UK

Antonio Buño Soto, Pathology Department, La Paz Hospital, Madrid, Spain

Peter P. Luppa, Institute for Clinical Chemistry and Pathobiochemistry, Technische Universität München, Munich, Germany

Anthony Malpass and Adam Stretton, Becton, Dickinson and Company, Wokingham, UK

Ulf Martin Schilling, Department of Clinical Education, Test and Innovation, Linkoping University Hospital, Linkoping, Sweden

Kevin D. Rooney, Royal Alexandra Hospital, Paisley, UK

Andrei N. Tintu, Erasmus MC, University Medical Centre Rotterdam, Rotterdam, The Netherlands

electrolytes, haemoglobin, co-oximetry, and other parameters such as glucose, lactate, bilirubin, ionized calcium and ionized magnesium on one instrument.

BGA is recommended by the American Association for Respiratory Care and other cardiopulmonary care societies for evaluating a patient's ventilatory, acid-base and/or oxygenation status, for evaluating a patient's response to therapeutic interventions and for monitoring severity and progression of cardiopulmonary disease processes [4].

BGA is usually carried out in a POCT setting in a busy and stressful environment, such as the ED and the ICU, where time-critical clinical decisions are made in patient management. Several preanalytical aspects of POCT BGA are unique to this type of testing and the multiplicity of measured and calculated parameters amplifies the effects of potential preanalytical errors leading to wrong results that can have immediate negative impact on patient outcome.

Major risks arise from poor operator competency, lack of supervision, poor governance, failure to implement quality assurance processes, lack of understanding of the limitations of use and uncertainty on how to act on the results [5].

To address the growing concern surrounding preanalytical errors, we believe that there is need for a dedicated risk analysis template that unites the available literature, whilst offering a practical solution to respond to the requirements of the International Organization for Standardization (ISO) standards. ISO has developed quality systems to assess specific aspects of health services. The ISO 15189:2012 standard for clinical laboratories requires that the laboratory evaluates the impact of work processes and potential failures on examination results, as they affect patient care and safety, and that the laboratory modifies processes, to reduce or eliminate the identified risks, and documents decisions and actions taken [6]. The ISO 22870:2016 standard is specific for POCT and is based on ISO 15189:2012 [7]. As a result, ISO 15189:2012 requirements, including risk management, also apply to POCT. As described in these ISO documents, the POCT coordinator, designated by the laboratory, has a pivotal role in the organisation, realisation, and certification of user training as well as promoting awareness to users and care-givers about preanalytical errors in POCT and their severely negative impact on patient safety and care.

As appropriate tool we used FMEA (Failure Mode and Effect Analysis) to develop a proactive model that identifies preanalytical risks of POCT BGA, measures their potential impact on patient outcome, and can be used to monitor corrective actions, with the goal to diminish risks. FMEA is a well-known tool for the analysis of process failures in many fields, that is also applicable for use in healthcare

[8, 9]. The proposed model includes key performance indicators (KPIs) and we also briefly describe the use of Risk Ranking Tables. KPIs and Risk Ranking Tables are complementary or alternative ways to monitor the effect of corrective actions [10, 11]. To the best of our knowledge, there is no other literature proposing a specific risk analysis for POCT BGA.

Materials and methods

A multidisciplinary team, composed of laboratory and clinical staff from different European countries, actively involved in BGA, designed the FMEA template. It was built in a Microsoft Excel spreadsheet and was informed by a combination of focus group discussions involving the team members and data from published literature [12–32]. The FMEA risk analysis procedure is schematically represented in Figure 1. The process steps involved in the pre-analytical phase of BGA are listed in the proposed model, as well as the errors that can occur whilst performing these steps (potential failure mode), the possible consequences of these errors (potential failure effect), their potential causes, and examples of potential preventive and detection measures that can be undertaken to avoid the errors (current controls). In accordance with De Vries et al., a scale from one to four was proposed to score probability of failure occurrence (OCC) severity of failure (SEV) and probability of failure detection (DET) per potential failure mode [9] (Tables 1A–1C). SEV, OCC, and DET are used to calculate the risk priority number (RPN = SEV × OCC × DET) [11]. The proposed model considers the classical blood gas parameters: arterial partial pressure of oxygen (PaO_2), arterial partial pressure of carbon dioxide ($PaCO_2$), pH, measured or calculated arterial oxygen saturation (SaO_2), calculated bicarbonate (HCO_3^-) and base excess (BE). These parameters can be reported on all blood gas analysers. The fraction of inspired oxygen (FiO_2) and the patient's body temperature can be introduced for calculation of PaO_2/FiO_2 and the alveolar-arterial gradient (A-a), and for temperature correction of pH and blood gas values respectively. Electrolytes such as sodium (Na+), potassium (K+) and chloride (Cl−) with calculated anion gap (AG), ionized calcium (Ca++), metabolites such as glucose (GLUC), lactate (LAC), bilirubin (BIL), and haematological parameters such as haemoglobin (Hb), haematocrit (Hct) and foetal haemoglobin (HbF) were also included as they can be measured by most blood gas analysers. Ionized magnesium (Mg++) is exceptionally measured and was also included, as were parameters measured by means of co-oximetry: oxygen saturation of haemoglobin (sO_2), oxyhaemoglobin (O_2Hb), deoxyhaemoglobin (HHb), carboxyhaemoglobin (COHb) and methaemoglobin (MetHb). Table 2 shows a snapshot of the FMEA model, containing the 12 process steps for BGA that were identified and one example per process step. Table 3 shows an example of a Risk Ranking Table calculated according to XFMEA [11]. In this example, the team performing the risk analysis decided 1° that a SEV = 1 does not need any corrective action, regardless of the value for OCC, 2° that a high severity (SEV = 4) will always give rise to a corrective action, whatsoever value for OCC, and 3° that a SEV of two or three will need corrective action only when there is a low probability of detection (DET ≥ 3). Table 4 shows the difference between monitoring the result of corrective actions after two revisions by means of the RPN value, with a user-defined threshold for RPN ≥ 10,
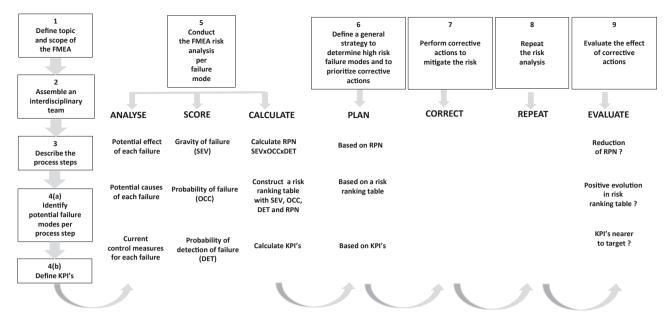
Figure 1: Schematic representation of risk analysis by means of failure mode and effects analysis (FMEA), key performance indicators (KPI) and Risk Ranking Tables.

Table 1A: Scoring table for severity of failure (SEV), according to De Vries et al. [9].

SEV score	1	2	3	4
Severity scale	Minor event	Moderate event	Major event	Catastrophic event
Patient outcome	Neither injury nor increased length of stay or increased level of care	Increased length of stay or increased level of care for one or two patients	Permanent lessening of body functioning, disfigurement, surgical intervention required, increased length of stay of three or more patients	Death or major permanent loss of function or suicide
Staff outcome	First aid treatment only with no loss of time or restricted duty injuries or illness	Medical expenses, lost time or restricted duty injuries or illness for one or two staff	Hospitalization of one or two staff, or three or more staff experiencing lost time or restricted duty injuries or illnesses	One death or hospitalization of three or more staff
Equipment outcome	Damages < 10,000\$ without adverse patient outcome	10,000\$ ≤ damages < 100,000\$	100,000\$ ≤ damages < 250,000\$	Damages ≥ 250,000\$

Table 1B: Scoring table for probability of failure occurrence (OCC), according to De Vries et al. [9].

OCC score	1	2	3	4
Probability scale	Remote	Uncommon	Occasional	Frequent
	Unlikely to occur; may happen sometime in 5–30 years	Possible to occur; may happen sometime in 2–5 years	Probably will occur; may happen several times in 1–2 years	Likely to occur immediately or within a short period, may happen several times a year

Table 1C: Scoring table for probability of failure detection (DET).

DET score	1	2	3	4
Detection scale	Absolute certainty	High	Low	Absolute uncertainty
	Always detected	Moderately high to high probability of detection (detected in ≥50% of cases)	Moderately low to low probability of detection (detected in <50% of cases)	Never detected

Table 2: process steps of the failure mode and effects analysis (FMEA) POCT BGA, with examples of potential failure modes, current controls and key performance indicators (KPI) per process step.

No.	Process step	Potential failure mode	Potential failure effect	SEV	Potential causes	OCC	Examples of potential preventive measures	Current controls			Definition of KPI	KPI	User defined criterium for KPI
								Examples of potential detection measures	DET	RPN			
1.	**Patient checks to be performed before starting the collection procedure**												
1.1.	Check whether patient has aberrant hemoglobin, e.g. sickle cell anemia, fetal hemoglobin	Erroneous procedure in this particular type of patient	Inaccurate cooximetry readings. Falsely increased carboxyhaemoglobin. INCORRECT PATIENT DIAGNOSIS/TREATMENT	4 SEV refers to patient-related outcome	Insufficient patient information. High oxygen affinity hemoglobins have altered dissociation curves and discrepant apparent oxygen saturation		Training. Effective patient history taking/hand over. Perform measurement <15 min after blood collection if plastic syringe is used, or else use glass syringe	Link with ICD code			Percentage of samples from patients with the appropriate ICD code that were not measured in time/total number of samples		
2.	**Entry of the blood gas request**												
2.1.	Manual entry of the blood gas request on the instrument	Missing tests or wrong tests performed on the instrument	Need for repeat sample.	2 SEV refers to combined patient and staff related outcome	Errors during manual entry of the requested tests on the instrument		Electronic request system. Bidirectional communication between LIS and instrument						
3.	**Identification of patient and user**												
3.1.	**Labelling of sample container (syringe) with patient identifying number or barcode before proceeding to blood collection**												

Table 2: (continued)

No.	Process step	Potential failure mode	Potential failure effect	SEV	Potential causes	OCC	Examples of potential preventive measures	Examples of potential detection measures	DET	RPN	Definition of KPI	KPI	User defined criterium for KPI
3.1.1.	**Manual identification of the sample**												
3.1.1.1.	Identify patient and label sample manually	No identification	Syringe cannot be labeled. Need for repeat sample.	2 SEV refers to combined patient and staff related outcome	Unidentified unconscious patient			Dummy code			Percentage of samples with dummy code/total number of samples		
3.1.2.	**Barcode label printed after identification of the patient by reading patient's barcode identifier on wrist band**												
3.1.2.1.	Read barcode on wrist band and print label for sample	No identification	Syringe cannot be labeled	1 SEV refers to patient-related outcome	No wrist band		Manual identification with use of positive patient identifiers, name, date of birth, electronic ID via national number (e.g., NHS number)	Dummy code			Percentage of samples with dummy code/total number of samples		
3.2.	**Labelling syringe**												
3.2.1.	Labelling syringe with request/sample ID	Wrong identification	Wrong label on sample, wrong (switched) blood gas results. INCORRECT PATIENT DIAGNOSIS/TREATMENT. Need for repeat sample	4 SEV refers to combined patient and staff related outcome	Barcode/label applied from other patient's test request		SOP, training	Register misidentified samples			Percentage of misidentified samples/total number of samples		
3.3.	**Unique barcode on syringe**												

Table 2: (continued)

No.	Process step	Potential failure mode	Potential failure effect	SEV	Potential causes	Current controls					Definition of KPI	KPI	User defined criterium for KPI
						OCC	Examples of potential preventive measures	Examples of potential detection measures	DET	RPN			
3.3.1.	Read unique barcode on syringe and link to patient barcode	No identification	Blood gas results cannot be used. Need for repeat sample	2 SEV refers to combined patient and staff related outcome	Barcode on syringe not linked to patient ID		Warning by instrument, SOP, training	Register unidentified samples			Percentage of unidentified samples/total number of samples		
3.4.	**Identification of the user**												
3.4.1.	Staff verification of ID before injecting the sample (for audit trail)	Lack of staff ID in procedure, result not traceable to user.	Errors in process are not traceable to staff member, patient results go to wrong staff member, negligence or errors not detected	1 SEV refers to combined patient and staff related outcome	Staff do not have ID badge and use/switch ID badges from/with other staff, or identify themselves on paperwork as other staff members.		State registration, training, SOP	Register samples with missing user identification. Warning for missing user identification by instrument			Percentage of samples with missing user identification/total number of samples		
4.	**Preparation of the patient**												
4.1.	Allow time (at least 15–30 min) for stabilization following a change in position of the patient before collecting blood	Patient not correctly prepared	Wrong blood gas results. INCORRECT PATIENT DIAGNOSIS/TREATMENT. Need for repeat sample	4 SEV refers to combined patient and staff related outcome	Blood taken <15 min after change in position of the patient as postural changes affect ventilatory rate and depth		Training						
5.	**Circumstantial external factors**												
5.1.	Disasters, pandemics, leading to a vast increase of ICU admissions	Patients not correctly prepared, erroneous identification, erroneous measurements	Wrong blood gas results. INCORRECT PATIENT DIAGNOSIS/TREATMENT. Need for repeat sample	4 SEV refers to combined patient and staff related outcome	Increased workload		Disaster and pandemic training, effective multidisciplinary team communications, delegation of tasks						
6.	**Patient characteristics**												

Table 2: (continued)

No.	Process step	Potential failure mode	Potential failure effect	SEV	Potential causes	OCC	Examples of potential preventive measures	Examples of potential detection measures	Current controls			Definition of KPI	KPI	User defined criterium for KPI
									DET	RPN				
6.1.	Remove traces of benzalkonium compounds (used as disinfectant)	Incorrect procedure	Invalid Na+ and/or Ca++. INCORRECT PATIENT DIAGNOSIS/TREATMENT. Need for repeat sample. Possible diagnostic delay with delay in therapeutic intervention.	4 SEV refers to combined patient and staff related outcome	Insufficient patient information. Instrument flag for interference with benzalkonium compounds neglected by the user		Training	Instrument flag for interference with benzalkonium compounds				Percentage of samples with instrument flag for interference with benzalkonium compounds/total number of samples		
7.	**Infection risk**													
7.1.	Check for infection in the patient when sampling blood	Infected user	No effect on patient results	4 SEV refers to staff related outcome	Needle exposure		Safe needles, training	Register needle exposures				Percentage of reported needle exposures/total number of samples		
8.	**Type of sample**													
8.1.	**Select the appropriate syringe**	Wrong/inadequate syringe	Wrong results. INCORRECT PATIENT DIAGNOSIS/TREATMENT. Need for repeat sample	4 SEV refers to combined patient and staff related outcome	Lack of training, distraction, stress. Inappropriate anticoagulants (other than heparin) such as oxalate and EDTA can interfere with electrolyte or enzymatic measurements by chelating divalent cations		Staff training	Register samples in wrong syringes				Percentage of samples in wrong syringes/total number of samples		
8.2.	**Arterial blood**													
8.2.1.	Arterial puncture	Erroneous procedure	Wrong results. INCORRECT PATIENT DIAGNOSIS/TREATMENT. Need for repeat sample	4 SEV refers to combined patient and staff related outcome	Contamination with venous blood		Training, skilled staff							

Table 2: (continued)

No.	Process step	Potential failure mode	Potential failure effect	SEV	Potential causes	OCC	Current controls							
							Examples of potential preventive measures	Examples of potential detection measures	DET	RPN	Definition of KPI	KPI	User defined criterium for KPI
8.3.	Venous blood												
8.3.1.	Peripheral vein	Wrong sample type if pO2 and pCO2 are clinically important in this patient	Reduced pO2, possibly erroneous pCO2. INCORRECT PATIENT DIAGNOSIS/TREATMENT. Need for repeat sample.	4 SEV refers to combined patient and staff related outcome	Large variability of the arterio-venous difference for pO2		Training						
8.4.	Capillary blood												
8.4.1.	Heel puncture	Erroneous procedure	Reduced pO2, possibly erroneous pCO2, increased K+. INCORRECT PATIENT DIAGNOSIS/TREATMENT. Need for repeat sample.	4 SEV refers to combined patient and staff related outcome	Insufficient dilation of arterioles		Training, skilled staff	Comparison with results obtained in the central laboratory			Percentage of samples with clinical significant difference between POCT and central laboratory results/ total number of samples that were measured in both settings		
9.	Sample collection												
9.1.	Device storage	Alteration of additive or syringe materials	Altered additive stability, physical characteristics of the syringe leading to aberrant test results. INCORRECT PATIENT TREATMENT	4 SEV refers to patient-related outcome	Device stored outside of manufacturer's stated conditions		Training, resilient product specification						
10.	Sample transport												
10.1.	Transport temperature	Transport at 0 °C of plastic tube	Increased or decreased pO2 (dependent on patient's pO2), increased K+. INCORRECT PATIENT DIAGNOSIS/ TREATMENT. Need for repeat sample	4 SEV refers to combined patient and staff related outcome	Temperature too low for plastic tube: promotes movement of ambient air across plastic		Training, logistics, point-of-care location of analyser						

Table 2: (continued)

No.	Process step	Potential failure mode	Potential failure effect	SEV	Potential causes	OCC	Examples of potential preventive measures	Examples of potential detection measures	DET	RPN	Definition of KPI	KPI	User defined criterium for KPI
								Current controls					
11.	Choice of blood gas instrument												
11.1.	Injection of the sample	Incorrect procedure	Intra-patient "volatility" of blood gas and electrolyte results when samples of same patient are measured on different instruments	2 SEV refers to patient-related outcome	Discrepancies between results of different blood gas instruments when the instruments are not properly managed		SOPs should indicate which instrument(s) should be used for the ward and which instruments should be used as back-up. All instruments should be controlled and aligned. Differences between instruments should be kept as low as possible. If known differences cannot be avoided, the patient should be monitored with the same instrument	Monitor differences between instruments by means of QC results			Percentage of time instruments show clinically significant differences		
12.	Injection of the sample												
12.1.	Active injection of the sample (not on all instruments)	Incorrect procedure	Increased pO2 and K+. INCORRECT PATIENT DIAGNOSIS/TREATMENT. Need for repeat sample. Can cause damage to the instrument	4 SEV refers to combined patient, staff, and equipment and facility related outcome	Excessive injection pressure (on particular instruments)		Training	Manufacturers of blood gas analyzers should develop methods to detect hemolysis in whole blood (currently hemolysis does not generate a specific flag for hemolysis on any instrument)					

Table 2: (continued)

No.	Process step	Potential failure mode	Potential failure effect	SEV	Potential causes	OCC	Examples of potential preventive measures	Examples of potential detection measures	DET	RPN	Definition of KPI	KPI	User defined criterium for KPI
												Current controls	
12.2.	Active injection of the sample (not on all instruments)	Incorrect procedure	Infection risk for users. Can cause damage to the instrument	3 SEV refers to combined equipment and facility-related and staff-related outcome	Blood spillage		Training						

SEV, gravity of failure; OCC, probability of failure; DET, probability of failure detection; RPN, risk priority number.

or by means of a Risk Ranking Table using the same conditions as applied in Table 3.

Results

The FMEA model is provided as an open Excel template (Supplemental Material, File 1).

Users should decide which process steps, risks, and proposed controls for prevention and/or detection of the different failure modes apply to their setting and patient population and adapt the model accordingly. As SEV is relatively independent of settings and patient populations, a score for SEV is proposed. SEV scores can refer to purely patient-, staff-, or equipment/facility-related outcomes (Table 1A), or to a combination of two or all three of these categories. In the FMEA template the distinction is made by means of a colour scheme. A minority of SEV scores purely refers to patient outcomes. Most SEV scores refer to combined patient- and staff-related outcomes. Patient related outcomes are mostly increased test turnaround time (TAT), potentially wrong diagnosis with diagnostic delay resulting in a wrong or delayed therapeutic intervention, potential increase of the hospital length of stay (LOS) and temporary or permanent damage to the patient. Staff-related outcomes in these cases either relate to infection risk for the user or to an enhanced workload caused by the need for a repeat sample. Equipment or facility related outcomes relate to temporary or permanent instrument damage/instrument shutdown due to preanalytical errors. OCC and DET are dependent on settings and patient populations and should be scored by the performers of the risk evaluation to obtain a calculated RPN that is specific for their setting and patient population. The user should also determine the cut-off for the RPN that will trigger corrective actions, aiming at a reduction of OCC (preventive measures) and/or DET (detection measures). The % reduction of RPN after corrective actions is a measure of their success.

The template proposes several KPIs, that can also be used to monitor the effect of corrective actions. Data needed to calculate KPI's can be retrieved from most lab information systems (LIS) or from the blood gas instrument. More complicated KPI's including clinical data (e.g., ICD codes) need more advanced data-mining tools. Users should decide which KPI's are feasible and applicable to their setting and patient population.

An additional way to manage corrective actions is the use of Risk Ranking Tables, wherein the initiation of corrective actions depends on user defined thresholds for OCC, SEV, and DET. The simple example of a Risk Ranking Table shown in Table 3 excludes corrective actions for

Table 3: Example of a risk ranking table constructed according to XFMEA methodology.

		SEV			
		1	2	3	4
O	1		4*	3*	
C	2		3*	3*	
C	3		3*	2*	
	4		2*	1*	

*The numbers in the cells represent DET

🟩	No corrective action required.
🟧	Corrective action always required.
🟨	Corrective action required if the DET >= a given number.

For this example, the decisions taken by the team performing the risk analysis were: If SEV = 1, then corrective action is never required. If SEV = 4, then corrective action is always required. If 1 < SEV < 4, then corrective action is required if DET ≥ 3. SEV, Severity of failure; OCC, probability of failure occurrence. The numerical values in the cells represent probability of failure detection (DET).

Table 4: Example of the use of a RPN Risk Ranking Table to monitor the effect of corrective actions, showing the difference between monitoring the effect of corrective actions by means of a Risk Ranking Table on one hand and by means of reduction in RPN on the other hand.

	SEV	OCC	DET	RPN	Reduction in RPN
Initial risk analysis	4	3	3	36	
Revision 1	4	2	3	24	33%
Revision 2	4	1	2	8	67%

For this example, the initial risk analysis and both revisions were performed by the team from Table 3. The cut-off for the RPN was set by the team at ≥10 (no corrective action needed when RPN < 10). After revision #1, corrective action is still needed, both according to the RPN and to the Risk Ranking Table (cfr. Table 3). After revision #2, corrective action is no longer needed according to the cut-off set for the RPN. After revision #2, corrective action is still needed according to the Risk Ranking Table, as SEV = 4. SEV, Gravity of failure; OCC, probability of failure; DET, probability of failure detection; RPN, Risk Priority Number.

errors with low SEV, low OCC and high probability of detection (low DET). When, over time, corrective actions have diminished the risk for errors with high SEV, high OCC and high DET, the user can lower the thresholds to also tackle errors with low SEV and/or low OCC and/or high probability of detection. The difference between monitoring the result of corrective actions by means of RPN or by means of a Risk Ranking Table is shown in Table 4. Based on RPN, corrective action would no longer be needed in this example after the second revision, as the RPN was lower than the threshold set by the user. However, according to the conditions set for the Risk Ranking Table, additional actions to lower DET and OCC would still be needed.

Discussion

Preanalytical POCT errors cause a considerable human, clinical and economic burden. This was recently demonstrated by Kazmierczak et al., who studied the impact of preanalytical POCT errors on productivity in a US ED [33]. The authors observed erroneous results in 6% of 15,479 i-STAT cartridges, of which 372 were unusable results. Errors for 163 out of 563 cartridges were definitely classified as originating from poor sample quality/improper sample handling. TAT and LOS were significantly longer with erroneous results. Direct costs over 2 years were 45,000 US$ and indirect cost was estimated between 486 and 729 h in avoidable nursing labor [33]. This study by Kazmierczak

illustrates the need for proper risk management of the preanalytical phase in POCT.

FMEA is a generally accepted method for proactive risk evaluation, applicable in healthcare and more specific for clinical laboratory measurements [34–38]. It is important to emphasize that the FMEA model proposed in this article covers a broad range of work environments, as it was designed by a group of lab professionals and clinical staff from different European countries and with different backgrounds and profiles.

A recently learned lesson is that disasters, such as the COVID-19 pandemic, affect the way POCT is performed and increase the risk for pre-analytical errors. The vast number of ICU admissions caused by SARS-CoV-2 infections resulted in an increased workload with high and continuous stress. As a result of delocalization and conversion of non-ICU beds to ICU beds, ICU staff worked in non-familiar areas and non-ICU staff, who lacked training and experience, worked within an ICU setting. Off-line installation of extra blood gas instruments and open access of the instruments were additional risks. In these conditions it is almost certain that errors have been underreported. The presented FMEA covers these particular risks under "circumstantial external factors", which is not per se a process step. To avoid the need for tracing the various causes of error due to the major risks associated with difficult circumstances, and to establish appropriate indicators and plan suitable strategies, users can choose to build a separate and more detailed FMEA for disasters departing from the presented model.

When an organization considers the FMEA type of risk evaluation, the analysis should be performed by an interdisciplinary team including lab manager(s), lab personnel, POCT coordinator(s), nurses, and other clinicians. The model that is presented here is constructed as a tool to manage risk, which can also be helpful when designing and implementing a new BGA network, but it is clearly not meant for 'daily use'. Once the initial table has been filled in, the team should decide which risks are dealt with on a priority basis. Urgent issues need prompt action(s) and in this case the team must decide how soon the relevant part of the exercise has to be repeated to measure their effectiveness. In the absence of urgent issues, the full FMEA exercise can be repeated periodically (e.g., every two to three years) to evaluate the overall effect of the measures taken. Appropriate use of the template offers a practical solution to answer the requirements of the ISO standards, thereby answering its main aim, being the improvement of patient safety and patient care by diminishing the risks [6, 7].

While many of the pre-analytical steps in BGA are common to all laboratory tests, such as accurate specimen labelling, some are unique to this testing because of the physicochemical and biological properties of the analytes being measured. Biologic variation of some blood gas parameters is very low (e.g., pH, Na+) and even little error cannot be tolerated in order to interpret small but clinically relevant changes. Hence, the preanalytical steps must be perfectly followed and performed to ensure that the patient receives appropriate and timely therapy in response to correct analytical results.

For example, the preparation of the patient that requires a waiting time of 15–30 min after repositioning before taking a blood sample is often not applied [15]. As patient care is prioritised based on need, the risk of "skipping 15 min" is very high. Underlying reasons might be elucidated further but generally can be seen as a combination of departmental culture and (experienced) workload, insufficient knowledge and general stress, i.e. both internal and external factors. This can be addressed by both specific training regarding BGA and disaster training/ stress management, and by quality control by local leadership. Interestingly, this error is more common when the ED or ICU is working with the normal flow or limited crowding, as moderate overcrowding will automatically provide the 15 min needed. As is shown with this example, but also throughout the whole template, the importance of training and ensuring best use of nurses' time by streamlining preanalytical processes cannot be overemphasised [39].

The importance of local factors was demonstrated by Auvet et al. [40]. By comparing BGA results for electrolytes and haemoglobin in a cardiac surgery operating room, a neurosurgical ICU and a polyvalent ICU, the authors show that identical analysers provided results of varying quality, depending on the local constraints of the ICUs. One of the most important findings of this study was that a stringent quality management can overcome these issues [40].

According to the guidelines of the American Association for Respiratory Care, the "gold standard" sample for BGA is arterial blood, collected by needle puncture of an artery or via an indwelling arterial catheter [4]. Capillary samples are not recommended to determine the oxygenation status of the patient, nor are central or peripheral venous samples recommended as a substitute for arterial blood measurement of pO_2, pCO_2, and pH. On the other hand, corrected central venous pH, pCO_2 and bicarbonate have been shown to provide clinically accurate results and, for many patients, non-invasive pulse oximetry may be sufficiently accurate to determine the patient's oxygenation status, avoiding the risks of an arterial puncture [12, 31]. Central or peripheral venous samples can be used for the fast measurement of electrolytes and metabolites,

and to monitor the acid-base balance of patients (although severity of acidosis or alkalosis may be under- or over-estimated) [12, 31].

A factor that may be overlooked is the importance of continuous *in vitro* cell metabolism for the accuracy of BG measurements. PaO_2 for instance is affected by several factors, including the number of oxygen-consuming blood cells. The rate of *in vitro* oxygen consumption was found to be proportional to white-blood-cell count, platelet count and reticulocyte count [23]. Routine precautions, such as measuring the sample within 15 min (maximum 30 min), are not sufficient to prevent spurious hypoxemia due to significant *in vitro* oxygen consumption in the context of hyperleukocytosis (white-blood-cell count $> 100 \times 10^9$/L) or extreme thrombocytosis (platelet count $> 2000 \times 10^9$/L) [23]. Mature erythrocytes on the other hand lack mito-chondria and contribute little to the total *in vitro* oxygen consumption, but they do metabolise glucose by anaerobic glycolysis and as a result, delayed measurement can cause spurious hypoglycaemia. Although the performance of small dedicated POCT devices for blood glucose measure-ment in critically ill patients has improved over time, BGA remains the golden standard for blood glucose measure-ment in these patients [25]. Incorrect POCT glucose mea-surement can be an important cause of falsely elevated glucose when using capillary blood, due to peripheral oedema. Treatment of these patients for hyperglycaemia can lead to serious hypoglycaemia, therefore arterial or venous blood samples are preferred for blood glucose measurement by means of blood gas analysers [25]. Brennan et al. reported that significant glucose contamination (3 mmol L^{-1} ± 3.4) was detected in all open arterial line sys-tems up to an aspiration volume of five times the dead space, while no samples from the closed systems recorded glucose concentration >1 mmol L^{-1} [26]. The same authors also found that recommended minimal discard volumes are inadequate in the presence of glucose in the flush solution and can lead to high blood glucose readings, inappropriate insulin use, and iatrogenic neuroglycopenia. Closed-loop arterial sampling systems could be the universal solution [26].

Some substances that interfere with BGA measure-ments are mentioned in the template, e.g., salicylates and halogen ions, such as bromide, interfere with chloride measurement, while glycolic acid and D-lactate interfere with L-lactate measurement and benzalkonium interferes with electrolyte measurement [18, 20, 21]. Other molecules, such as ascorbic acid, bilirubin, citrate, EDTA, ethanol, heparin, glucose, paracetamol, salicylate and urea are also listed in BGA reference manuals as potentially interfering with lactate measurement.

In some instances, interchangeable use of electrolyte results (especially sodium) from direct ion-selective elec-trodes (dISE) – used in BGA – and indirect ion selective electrodes (iISE) – used in most routine central lab in-struments – is not advisable, especially in a setting of hyperproteinaemia or hyperlipidaemia [32].

Several rating scales can be used to score SEV, OCC and DET (e.g., 1–4, 1–5, 1–10 etc.) but, as the scores are multiplied to obtain RPN, the same rating scale should be applied to SEV, OCC, and DET to avoid the appearance of skewing the resulting RPN [41]. In the present template a linear rating scale with consecutive numbers (1–4) was chosen. Alternatively, and as long as the same rating scale is applied to all three components, non-consecutive numbers can be chosen by the user (e.g., 1, 3, 5, 7), as they may allow more distinction between ratings and cause less debate amongst team members or, when the team wants to put more emphasis on the higher scores, a non-linear scoring scale can also be utilized (e.g., 1, 4, 9, 16) [41].

Only SEV is scored in the template, while OCC and DET are not, as they are highly dependent on the test setting and on the patient population and in any case, they should be scored by the multidisciplinary team. For example, OCC and DET will be different in a primary community health centre as compared to a secondary district general hospital and certainly as compared to a third line university hospital or specialized hospital e.g., trauma centre, cancer centre. OCC and DET will also differ whether the instruments are stand-alone or connected to a management software and a lab in-formation system, whether patient identification is manual or automated and whether results are automatically transmitted to the patient's electronic health record. When OCC and DET are scored for local settings and patient populations, the calculated RPN can be applied to determine the sequence and prioritise which risks need to be addressed. Therefore, the team should determine the cut-off for the RPN that triggers corrective action. After implementing changes to decrease the occurrence of errors, the RPN should be re-calculated to measure their positive effect [41]. Sometimes choices have to be made, as it is not always possible to reconcile different corrective actions e.g., although plastics are partially gas permeable as opposed to glass, glass syringes were largely replaced by plastic syringes due to safety concerns.

The exclusive use of RPN values for prioritisation of failures that need corrective actions should be considered with caution. As the scores for SEV, OCC, and DET are multiplied, small changes in one score can lead to large changes in RPN. For example, a failure mode with high DET, high OCC but low SEV would be prioritized the same as a failure mode with high DET, low OCC but huge SEV,

despite having different risk implications [9, 42]. It may therefore not be appropriate to give equal weight to the three ratings that comprise the RPN. An organization may consider issues with high SEV and/or high OCC ratings to represent a higher risk than issues with high DET ratings. The analysis team may then decide to initiate a corrective action anyway because of the very high severity of the potential effect of the failure, even when the RPN is not high enough to trigger corrective action. In this regard the team may develop a Risk Ranking Table in addition to – or instead of – using RPN values for prioritization of the need for corrective actions [11]. Risk Ranking Tables identify whether corrective action is required based on the combination of individual values for SEV, OCC, and DET, thereby allowing for more nuance as compared to the use of the RPN value for evaluating the effect of corrective actions. Another way to monitor corrective actions is the use of KPIs [10]. KPIs are quantifiable measures used to evaluate whether objectives for performance are met. We present a number of KPI's in our template. The team should decide which KPI's are feasible and applicable to their setting and patient population. The team should also define criteria for these KPI's, below which no corrective action is needed. The percentage change in the chosen KPI's obtained after corrective actions is a measure for their effect. Introducing a priority scale for KPI's could facilitate their gradual introduction into routine practice, by starting with a "mandatory" (score 1) and ending with a "valuable" (score 4) score, as was proposed by Plebani et al. for the reduction of preanalytical errors in the clinical laboratory [43].

Limitations of the study

The proposed template is based on a combination of data from published literature and the experience of the team members and their collaborators, but the template has not yet been clinically validated. Although we tried to be as complete as possible, not only including common errors but also rarely occurring causes of error, some potential hazards and unicorns may have been overlooked.

Conclusions

The proposed FMEA analysis model responds to the practical necessity of having a risk analysis tool that can be used to design and implement a BGA network and to monitor its improvement over time, according to the requirements for accreditation and certification. However, this is not the only practical consequence. In fact, we hope that this initiative may lay the foundations for a single FMEA model that is widely applicable in various organisational contexts at international level. This shared model for proactive risk analysis could become a starting point for quality comparisons between organisations, thanks to the sharing of the same monitoring indicators, as it happens with laboratory errors [43, 44]. This would make the effort to carry out such analyses even more useful and significant, as it could lead to an assessment of the organisation against the average international performance, if not against shared standards (benchmark).

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