The Proxima System revolutionises blood gas analysis sampling

Up to 60% of all errors in blood gas testing occur in the pre-analytical phase

Up to 37% of pre-analytical errors in laboratory STAT (short turnaround time) testing are caused by provision of a deficient sample

### Sources of pre-analytical error

<table>
<thead>
<tr>
<th>Source of Error</th>
<th>The Proxima System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemolysed samples</td>
<td>Immediate sample analysis and no sample mixing required</td>
</tr>
<tr>
<td>Errors associated with anti-coagulation</td>
<td>Anti-coagulant not required</td>
</tr>
<tr>
<td>Low integrity blood samples</td>
<td>Repeatable high integrity blood samples present in the Sensor for analysis</td>
</tr>
<tr>
<td>Sample storage and transport</td>
<td>Arterial line tube fitted with captive syringe, no further manipulation required</td>
</tr>
<tr>
<td>Sample sedimentation</td>
<td>Immediate sample analysis precludes sedimentation</td>
</tr>
<tr>
<td>Errors in patient identification</td>
<td>Results displayed at patient’s bedside</td>
</tr>
<tr>
<td>Sample contamination</td>
<td>Blood sample kept in a closed air-free system at all times</td>
</tr>
</tbody>
</table>

The Proxima System mitigates:

- Patient misdiagnosis
- Incorrect patient treatment
- Delays in diagnosis
- Need for resampling
Addressing common pre-analytical errors associated with arterial blood gas analysis using the Proxima System
Dr Jess Fox & Dr Gavin Troughton, Sphere Medical Limited

Introduction
Arterial blood gas analysis is common in critical care settings, where the results almost always have the potential to dictate an immediate or urgent response. The pre-analytical phase of analysing a clinical sample refers to all of the activities that occur prior to the sample’s insertion into the analytical instrument. These steps must be carefully performed to ensure that the patient receives accurate test result and consequently appropriate and timely treatment.

Many of the pre-analytical steps in arterial blood gas analysis are analogous to other laboratory tests, e.g. accurate sample labelling. However, some pre-analytical steps and potential sources of error are unique to blood gas analysis due to the physicochemical properties of the analytes being measured. This document explores how and why the pre-analytical errors occur along with the impact of the error on the analyte levels in the blood sample. We also consider the Proxima System, an on-demand arterial blood gas analyser that is designed to address many of the errors that can occur in the pre-analytical phase.

Incidence of pre-analytical errors
Pre-analytical processes tend to be more error prone than those later in the testing process as the specimen collection is a manual procedure, while analytical and post-analytical phases are often automated and consequently subject to reliable computer checks.

Pre-analytical errors in clinical chemistry occur in around 1-1.5% of all samples analysed1,2. They can result in patient misdiagnosis and incorrect patient treatment or a need for resampling3. Up to 60% of all errors in blood gas testing occur in the pre-analytical phase4. The incidence of commonly reported pre-analytical errors is shown in figure 1.

Common pre-analytical errors

Haemolysed samples
One of the most frequent pre-analytical errors to occur during the process of sample handling is haemolysis9, the result of which is the release of intracellular components into the plasma. Haemolysis can result when samples are handled vigorously e.g. high sample fill rate, vigorous sample mixing or dropping the sample container on the floor.

Sample haemolysis most affects the potassium ion measurement accuracy as the concentration is approximately 30 times greater in the intracellular compartment than in the plasma phase10. However, sodium, calcium and haemoglobin (Hgb) measurements can be affected, as summarised in table 1.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>0% haemolysis</th>
<th>0.5% haemolysis</th>
<th>5% haemolysis</th>
<th>10% haemolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>K⁺ (mM)</td>
<td>4</td>
<td>4.5</td>
<td>7.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Na⁺ (mM)</td>
<td>140</td>
<td>140</td>
<td>136</td>
<td>133</td>
</tr>
<tr>
<td>Ca²⁺ (mM)</td>
<td>1.2</td>
<td>1.2</td>
<td>1.1</td>
<td>1.0</td>
</tr>
<tr>
<td>Hgb (g/dl)</td>
<td>N/A</td>
<td>0.08</td>
<td>0.8</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Table 1: The consequence of haemolysis on the observed concentrations of K⁺, Na⁺, Ca²⁺ and Hgb9

Errors associated with anti-coagulation
Blood samples analysed on standard blood gas analysers require treatment with an anti-coagulant to avoid sample clotting, which can block the sample pathway of the blood gas analyser and affect the current and future samples11. The most common anti-coagulation errors are:

- **Delayed or inadequate mixing:** This can result in clotting of the sample. The associated processes will release potassium ions and can positively bias the potassium results4.

- **Wrong anti-coagulant:** Blood gas syringes use a dry balanced heparin to minimise the impact on the sample. Liquid heparin causes negative bias to all parameters by dilution and by binding the positive electrolytes4. The dilution effect varies depending on the volume of liquid heparin added vs the volume of blood gas sample, e.g. 0.05 ml liquid heparin added to a 1 ml blood sample (Hct 45%) will dilute the plasma phase by approx. 10%. Other anti-coagulants, such as EDTA, can change the pH of the sample as it is a weak acid.

Deficient samples
Up to 37% of pre-analytical errors in laboratory STAT (short turnaround time) testing are caused by provision of a deficient sample; this could be because the sample tube is empty, missing or inadequately filled or because...
the test request is missing. Such errors require additional samples to be drawn and cause delays in diagnosis.

**Sample storage and transport**

A blood gas sample which has been correctly collected and capped will continuously change during any delay between collection and analysis e.g. due to transport from patient to analyser or to availability of immediate analysis.

- **Metabolic effects:** Blood is a living tissue and metabolism continues within the sample after the blood is drawn. As a result, oxygen, carbon dioxide, pH, glucose and lactate levels are all affected.

- **Chilling:** If a prolonged (>30 min) time delay is anticipated before the sample is analysed, the use of glass syringes and storage in ice water is recommended. This slows down the metabolic effects, but can result in haemolysis and changing potassium levels. Furthermore, if a plastic syringe is used this can have a profound effect on the oxygen levels due to transport through the syringe.

- **Sample sedimentation:** Red blood cells separate from the plasma during storage and a heterogeneous sample will result if stored for even a short period of time. The effect of a heterogeneous sample on the bias will depend on which portion of the sample is measured. Apparently homogeneous samples which have been briefly mixed after just 10 minutes storage have been reported to under-read by 28%.

- **Transport:** Many hospitals use pneumatic tube systems to minimise the transfer time of samples from the patient to the laboratory. This can have a profound effect on the oxygen concentrations if there are any bubbles present in the sample.

**Errors in patient identification**

Incorrect or missing patient and/or sample identification are common pre-analytical errors that occur in blood gas testing. Errors can be caused by:

- Lack of patient identification and/or sample labelling
- Transcription errors due to manual data entry
- Lack of a dedicated procedure for identifying patient samples

Missing/incorrect information causes delays in sample analysis and can consequently lead to erroneous results, diagnosis and inappropriate treatment.

**Sample contamination**

The blood gas sample can become contaminated during the collection process:

- **Contamination from flush:** When sampling from an arterial line it is important to remove an adequate ‘discard volume’ to ensure the sample obtained for analysis is 100% blood. If an insufficient discard volume is removed, the sample will be contaminated with flush solution and the results affected.

- **Contamination with air:** Any air bubble in an arterial blood can alter the $pO_2$, $pCO_2$ and pH of the sample so that it no longer represents the patient’s status. Air bubbles with a relative volume of 0.5-1.0% of the sample may cause significant errors. Oxygen levels will tend towards atmospheric concentrations, i.e. there will be a decreased ability to detect profound hypoxia or hyperoxia. $pCO_2$ within the sample will fall (since atmosphere $pCO_2$ is very low), but the effect is less marked than the change in $pO_2$. As a direct consequence of the decrease in the $pCO_2$, pH will increase when arterial blood is exposed to air.

**The Proxima System and pre-analytical errors**

Proxima is a patient dedicated arterial blood gas analyser that allows critical care staff to obtain blood gas measurements without leaving the patient’s bedside – refer to figure 2.

The Proxima Sensor is integrated into the patient’s arterial line operating as a closed system to minimise blood handling and infection risk. During the sample measurement procedure, the user draws blood into the Proxima Sensor using a closed sampler syringe. Once the sample has been analysed, all blood is returned to the patient. Results are displayed on the bedside monitor.

The Proxima System has been designed to address many of the common pre-analytic and pre-analytical errors to deliver more reliable blood gas measurements. Table 2 presents the design features of the Proxima System and how common pre-analytical errors are addressed within this new medical device.
### Sources of pre-analytical error

<table>
<thead>
<tr>
<th>Error Type</th>
<th>The Proxima System is designed to address pre-analytical errors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemolysed samples</td>
<td>Sample analysis with the Proxima System is carried out immediately, avoiding risk factors for sample haemolysis such as storage on ice or vigorous mixing of the sample.</td>
</tr>
<tr>
<td>Errors associated with anti-coagulation</td>
<td>Blood samples analysed on Proxima do not require treatment with an anti-coagulant, thereby avoiding poor incorporation, the risk of dilution or inappropriate reagent choice.</td>
</tr>
<tr>
<td>Deficient samples</td>
<td>The Proxima System is designed so the user withdraws a fixed volume of blood which ensures a high integrity arterial blood sample is present in the Sensor for analysis. Since Proxima analyses the samples in situ, samples cannot be lost or test requests missed.</td>
</tr>
<tr>
<td>Sample storage and transport</td>
<td>The Proxima System is incorporated into an arterial line tube fitted with a captive syringe. When an analysis is performed, blood is drawn into the captive syringe until it is completely filled. The analysis then occurs without further manipulation of the sample which ensures errors associated with sample container choice are avoided. The Proxima System analyses samples within a few tens of seconds, during which there is no significant metabolism effect.</td>
</tr>
<tr>
<td>Sample sedimentation</td>
<td>The Proxima System measures the blood sample immediately after flowing through the Sensor and within a few tens of seconds, precluding the risk of sample sedimentation.</td>
</tr>
<tr>
<td>Errors in patient identification</td>
<td>The Proxima System is a patient dedicated in-line blood gas analyser displaying results directly at the patient bedside. This eliminates accidental misidentification or exchange of samples. The patient’s ID is captured in the Proxima System at the start of the episode of care and is automatically saved with all electronic records.</td>
</tr>
<tr>
<td>Sample contamination</td>
<td>The Proxima System is designed to accommodate a suitable discard volume within the line reservoir to ensure that a high integrity arterial blood sample is present in the Sensor for analysis. By returning the contents of the reservoir to the patient there is no reason to minimise the discard volume and risk a sample contaminated with flush. The Proxima System keeps the blood sample in a closed, air-free system at all times, thereby allowing the user to analyse blood samples at the patient’s bedside removing the impact of transport on sample quality.</td>
</tr>
</tbody>
</table>

**Table 2: Design features of the Proxima System that address common pre-analytical errors**

### References