

# POC testing and reporting of sodium, and other small molecules need modified IFCC source/type designations to improve operational efficacy and for clinically accurate, unambiguous reporting from LIMS and HIS.

Robert F Moran<sup>1</sup>

<sup>1</sup>Principal Scientist mviSciences, Chemistry and Physics (Ret), Wentworth Institute of Technology, Boston, MA

---

## Article Info

### Author of correspondence:

Robert F Moran, PhD, FCCM, FAIC, FIUPAC,  
Principal Scientist;  
E-mail: [RFMoran@mviSciences.com](mailto:RFMoran@mviSciences.com);  
Address:  
*mviSciences, LLC, Gilford, New Hampshire. 03249*

## Abstract

There seems to be a lack of clarity of meaning/understanding of names and symbols and ultimately of quantitative results of certain critical tests performed as a professional in the laboratory and healthcare environment and in the POC environment. Multiple observations of this phenomenon are derived from interactions by the author as a consultant for manufacturers of multicomponent blood gas systems, and through them to the end-users in hospitals, clinics, and point-of-care locations as well as with IT professionals in the health care industry. This causes unnecessary and time-consuming questioning of reported information in the critical care environment. We would recommend wider use of IFCC designations for quantified measurands and most especially specimen type/source plus incorporation of that information as a part of the quantity and name on analytical systems information management (ASIM)<sup>I</sup>, as well as by subsequent levels of information management including LIMS<sup>II</sup> and HIMS/IIMS<sup>III</sup>

Additionally, we suggest some modifications of the format and symbols to address the technology that uses a 'whole blood'(B) specimen to quantify concentrations of measurands, especially electrolytes in plasma and plasma/water. Both the sensors and the mode of system calibration are impactful for the clinical utility of the final value. The sensors, because of their 'membrane' detect a measurand in the plasma which is in equilibrium with the whole blood- without the need for other separation. Furthermore, since most, if not all, manufacturer's systems use calibration based on a CLSI<sup>IV</sup>-Inspired, NIST-developed Standard Reference Material<sup>V</sup> a reference material designed to ensure no difference among electrolyte results on patients with normal plasma water (i.e., Central Laboratory vs POC). Symbol modifications would include designating internal actions/calibration/calculations taken by the instrumentation that can aid in interpretation of values. These would be placed after the specimen type (e.g. (B)). Also, certain applications of such data to further calculations outside POC and Central Laboratory purview might be facilitated by the placement of the complete set of qualifiers as a parenthetical subscript to the quantity and measurand name/symbol, but this topic may be pursued elsewhere. We would promote wider consultation between

the IFCC and both member organizations and related medical professional organizations on these issues. Similar consultation should also exist between each central laboratory and institutional clinical professionals using the information and with the IT professionals who write the code to make the information available for laboratory, POCT and institution wide use.

<sup>I</sup> ASIM-Analytical System Information Management- The software/hardware package used by measuring devices in a linked analytical chain that allows for complete patient/specimen information and quality management data to be available independent of a LIMS.

<sup>II</sup> LIMS-Laboratory Information Management Systems.

<sup>III</sup> HIMS Hospital Information Management Systems, IIMS- Institutional Information Management Systems

<sup>IV</sup> CLSI- Clinical and Laboratory Standards Institute, Malvern, PA, USA, (Formerly NCCLS.

<sup>V</sup> SRM No.956d; Sodium in serum, National Institute of Standards and Technology OR National Bureau of Standards; U.S. Department of Commerce: Gaithersburg, MD.

**‘New’ technology-‘Old’ physiology:** Use of what may be referred to as ‘enhanced’ blood gas analyzers (eBGA’s)<sup>VI</sup> has brought about more frequent calls to the laboratory concerning result discrepancy especially for sodium ion and hemoglobin, among others. This assertion is based on personal observations made in my consulting practice for manufacturers and seems to center on differences between values obtained from central laboratory versus those from intensive care units (ICU) or Emergency departments. on specimens taken at the same time<sup>VII</sup>. I will focus here on just the electrolytes. Individual callers to the central laboratory about differences in values charted and the name of the value reported (e.g., ‘bicarbonate’ or ‘plasma bicarbonate’-are they the same thing?) may be assuaged after a brief investigation that finds the patient has a hyperlipidemia, dehydration, or more rarely a macroglobulinemia. However minor the delay (unless one is put on ‘hp;d’), there is still an obvious delay in finalizing evaluation and treatment of a patient. In addition, during our work with IT professionals as part of product development, we have observed that the naming of different measurands in the same manner makes it difficult to communicate with them as they design new reporting software. They, like many laboratory scientists and direct caregivers, are unfamiliar with the nuances in information about the changes imposed by the rapid advances of measurement technology. A simple example might be whether there is a difference between total carbon dioxide, carbon dioxide content and the molar concentration of carbon dioxide?<sup>VIII</sup>. When added up over time, these issues have the potential for economic and operational impact on the patient support team and are a quality management system issue. Consider, too, that when outside quality systems evaluators or governmental regulators assess testing patterns, there is likely to be a much broader requirement to evaluate patient populations and instruments performance -a costly exercise for both laboratory staff and direct-caregivers.

To improve result quality pro-actively, I might suggest some additions and slight changes to the symbolic reporting schemes currently recommended by the IFCC<sup>IX</sup>. For the blood gases, one is accustomed to using a parenthetic notation for specimen type and its source, following the quantity type and measurand identifier, Thus, for oxygen tension in arterial blood ideally one writes **pO<sub>2</sub>(aB)** as a **complete name** instead of the ‘**oxygen tension of arterial blood**’. This IFCC-based system of symbolic naming is fully adequate for those components of ‘blood gas’ that are, and necessarily measured in whole blood. However, the measurement technology intervened with the advent of the concurrent use in a ‘blood gas’ analyzer, of electrolytes and other small molecules.

<sup>VI</sup> ‘Enhanced’ blood gas analyzers are those designed in a linked analytical stream for measurands beyond the basic pH, pO<sub>2</sub> and pCO<sub>2</sub>,. including related entities such as electrolytes, and oximetry in various combinations.

<sup>VII</sup> Shives Prakash, Shailesh Bihari, Zahn Y Lim, Santosh Verghese Hemant, and Andrew D Bursten ) Concordance between point-of-care blood gas analysis and laboratory autoanalyzer in measurement of hemoglobin and electrolytes in critically ill patients; 2018 Jul; 32(6): e22425. Published online 2018 Mar 3.

<sup>VIII</sup> Answer-Nuanced differences only but watch out for reporting units.

<sup>IX</sup> Other additions might also be suggested for specimen type modifiers, based on the use and specimen types submitted-all leading to less ambiguity in the symbols-labels going to the patient record such as (vmB) for mixed venous blood-frequently used for follow-on calculations outside the laboratory. Here I will focus on just one issue.

**Analytical overview.** In the last several decades of the 20th century, the single most common first step in measurement of ‘blood’ electrolytes required a **quantitatively diluted** specimen of serum/plasma (i.e., the blood cells were already separated). This was followed by a determination of the intensity of the color characteristic in a reacted solution or in a gas- flame when the diluted specimen was aerosolized then injected into a flame of flammable gas. Ion-selective electrodes (ISE’s) were also used in place of the spectrophotometer or flame photometric sensor in systems designed for multi-specimen processing. Calibrators of precisely known concentration in water or buffered salt solution, **diluted similarly** to the plasma specimen were used to relate light intensity to concentration. **The flame emission technology (FAES)** specifically had been used for decades and was the basis of the reference ranges used by most clinicians. Dilution was required for both analytical and functional reasons. Calibrators were made in aqueous solutions and diluted similarly to the serum/plasma specimen with the same aqueous solution. **Ion selective electrodes (ISE’s)** first introduced for clinical use around the same period as the FAES becoming the reference method, had a sensitivity range that could be used on diluted

specimens but also enabled measurement on undiluted specimens. Elimination of the dilution step reduces pre-analytical preparation and enables faster turn-around time on individual specimens, but it was observed that the direct measurement resulted in a bias between undiluted ISE (frequently referred to as 'direct') and the reference method, especially for sodium. The observed consequence of ISE's being used on either plasma/serum alone, on whole blood or in blood gas systems would, on the average be a difference of about 7%. So, at a practical level, if ISEs were to be incorporated into 'blood gas systems', it was necessary to get the electrolytes, especially sodium, to agree, since confusion as to result meaning had no place in a critical environment. **Dilute before analysis.** The dilution is the crux of the issues associated with the technology. Initially the phenomenon was ascribed to simple methodological differences, but it then became recognized that it was because the ISEs were measuring the electrolytes of the medium in which they were dissolved-water-not in the serum/plasma/whole blood whereas the other methods involving dilution based the results on a reference calibrator made from water and pure sodium chloride. Measurement of the same specimen of blood, serum/plasma, resulted in an average of approximately 7% bias relative to the reference method (gravimetry or FAES), methods which had been used to develop reference intervals and had served as the standard for these critical measurands for decades. While this applies to all analytes dissolved in the plasma water, the significant effect is on sodium because of its typical value (140 +/- 5 mmol/L) and narrow acceptable range. A 7% bias represents the entire acceptable range<sup>x</sup>

<sup>x</sup> With a typical value for normal sodium of 140 +/- 5 mmol/L, a seven percent difference spans the whole range.

**'Undiluted' (or direct) analysis.** While research at the time had shown that differences between the direct, undiluted ISE and dilution (FAES) were not the result of measurement bias but rather to a pre-analytical bias induced by typical total protein concentration in the blood serum/plasma. Since most reported values were on systems that diluted the specimen first, whether in manual-procedure environments or on the multi-specimen analyzers most were calibrated based on a diluted aqueous standard and in general agreed with the FAES- reference method. Since the key was in the water concentration, any analysis using 'dilution' would agree with each other, even ones using ISE's. In addition to the analytical implications, there is a serious clinical implication- what about specimens containing significant high or low protein levels or high lipid levels! The ISE could explain the factitious low results for Na/K in macroglobulinemia and lipidemia's especially those found in uncontrolled diabetes<sup>xi</sup>.

<sup>xi</sup> A substantial set of references on all these points is found in the references of the CLSI documents referred to.

**Consensus Standardization.** As is recognized today, the ISE

technology introduced decades ago measures the electrolytes (and other small molecules) on both diluted and undiluted plasma. The Clinical and Laboratory Standards Institute (CLSI<sup>xii</sup> committees charged with examining the situation both analytically and clinically, developed a proposed, a tentative, and finally an 'Approved' standard, having published each for public review- a process taking in total several years. (See Bibliography). NIST, using the recommendations developed by CLSI<sup>xiii</sup>, then developed the Standard Reference Material (SRM 956d), available for use now, so that all systems can be calibrated to the same value for sodium, whether the specimen is diluted or not before analysis. In summary, the recommendation was to standardize all systems to avoid clinical confusion. This standardization was set to make specimens with normal plasma water concentrations agree without regard to method. This was done with the constructive agreement with the National Institute of Technology (NIST), since they prepare precise standards materials with protein/lipid amounts such that plasma water was 'normal'. By using this approach, confusion would be limited, and more importantly routine Na/K could be done on any system and the issue of discrepancy would not be an error in the method, but rather a significant difference in plasma water, the result of clinically pertinent conditions. CLSI, however, made no recommendation on reporting results as the morphing of 'blood gas' technology to use outside the laboratory was not considered at the time.

<sup>xii</sup> At the time CLSI was called the National Committee for Clinical Laboratory Standards (NCCLS)

<sup>xiii</sup> Recall that all major manufacturers were participants in the CLSI process.

#### **Solving our own problem in POC testing: The Point**

When all reporting of analytical values is the responsibility solely of the laboratory the solution is simplified. For example, if the result is from a high-volume system, likely a measurement involving dilution, one simply uses the appropriate IFCC symbol- but what is it? A bicarbonate would be  $c\text{HCO}_3^-$  and a sodium would be  $c\text{Na}^+$ . Simple, but insufficient. Consider that most authorities require that any value reported be identified by source and type. Why not have that information symbolically within the name of the quantity and measurand as placed on the patient record instead of in the record in various places? A bicarbonate reported from a blood gas system<sup>xiv</sup> would then be  $c\text{HCO}_3(\text{aBp})^{\text{xv}}$  [*i.e.*-molar concentration of bicarbonate in arterial blood plasma]. For a sodium measured on the same specimen, the symbol would be  $c\text{Na}(\text{aBp})$ . The designation of 'p' for plasma is based on what the analyzer does, not on the specimen type or source. Now there is no question about the source? Not quite--- given the differences in results possible in hospitalized populations. Consider that the eBGA is done immediately near the patient but that other specimens collected at the same time go to the main laboratory for less urgent testing that includes electrolytes, glucose, etc. as a

part of the ‘panel’ for metabolic screen. So, when fully charted there may be **two sets of electrolytes on specimens collected at the same time**—one typically done on a diluted specimen of plasma (central laboratory) one on an undiluted specimen of the plasma of the whole blood (POC, ICU, ED, etc.). They will usually agree but if not, how does one differentiate I believe the differentiation must begin with more complete naming within the IFCC system. The only complete pertinent symbol should include the notation with the reported result that shows the undiluted nature of the measurement itself, and thus the least ambiguous name for the reported quantity/entity. Since this occurs *post facto* to the specimen nature itself, additional designations should follow the ‘B’ if blood is the material. So, we can now have a final symbol for the sodium or bicarbonate which will be clear in its clinical and analytical meaning as shown in the table.

<sup>xiv</sup> Blood gas analyzers from the 1960’s through the current eBGA’s have been reporting ‘plasma bicarbonate’. While the issue is user understanding, the solution is proper result labelling.

<sup>xv</sup> Eliminate the charge symbol for simplicity, or even use ‘Bicarb’ instead of the chemical symbol.

	<i>Result Source</i>	<i>Bicarbonate</i>	<i>Sodium</i>
<b>1</b>	<b>POCT</b>	$c\text{HCO}_3$ (aBp <sub>u</sub> )	$c\text{Na}$ (aBp <sub>u</sub> )
<b>2</b>	<b>Central lab (best symbol)</b>	$c\text{HCO}_3$ (vBp <sub>d</sub> )	$c\text{Na}$ (aBp <sub>d</sub> )
<b>3</b>	<b>Central Lab (Acceptable)</b>	$c\text{HCO}_3$ (vB)	$c\text{Na}$ (vB)
<b>4</b>	<b>Central Lab (?)</b>	$c\text{HCO}_3$	$c\text{Na}+$

*Symbols in rows 1 and 2 when accompanied by the measured value and unit, exemplify unambiguous reporting. (The ‘u’ represents undiluted, the ‘d’ diluted, and ‘v’; venous.)*

In each symbol shown in the table, the ‘p<sub>u</sub>’ or ‘p<sub>d</sub>’ follows the ‘B’ to represent that the measurand is reported as a concentration in undiluted or diluted plasma. These examples clearly show the measurand, the specimen source and type, and that it was reported as a molar concentration in plasma that was diluted or undiluted<sup>xvi</sup>. That is, there should be no question about the meaning of the value reported- the necessary information is part of the name itself. Once coded into analytical system by manufacturers as well as by or LIMS suppliers, and in institutional software, this is a simple approach to providing complete and pertinent information in critical situations and minimizing confusion between results provided by different analytical systems.

<sup>xvi</sup> That is a new symbol ‘p<sub>u</sub>’ for plasma undiluted and for plasma, diluted ‘p<sub>d</sub>’.

**In conclusion**, these suggestions are both simple to implement and analytically sound and help to address the ambiguity and diagnostic/therapeutic advantage of direct ISE technology. The direct measuring BGA/Electrolyte system will be giving the physiologically correct result in all conditions. However, most electrolyte measurements on most patients the economical choice would be the large processing systems typically using a specimen dilution method which almost always is clinically sufficient and dependable. With the complete, unambiguous naming of the quantity, measurand and specimen characteristics, clinical assessment in critical situations will be enhanced.

**Some Supplemental Thoughts:** While from a scientific perspective some further suggestions are less important than the preceding, some may be critical to get full acceptance and use by the medical-professional users,

- Use standard typeface especially for the measurand symbol or name since special characters or ‘object’ files are not widely available/known.
- Other post-collection qualifiers, <sup>xvii</sup>should also be added following the ‘p<sub>u</sub>’.
- Recognize that since most measurements using eBGA’s will be on arterial blood, elimination of the ‘aB’ part of the symbol should be a laboratory/institution option allowed for in software coding, while absolutely retaining other source/type symbols as well as a symbol indicating unknown source.
- Expand the audience for the discussion to include not only the IT personnel who will implement this in hospital wide reporting systems but also to other medical specialties who may use the information for their own follow-on calculations (10, 14, 15).
- Parenthetic symbols may be subscripts to the quantity and measurand name especially if the quantity is used in follow-on calculations done by other professionals in the critical care team. From our examples -  $c\text{HCO}_3$  (aBpu) and  $c\text{Na}$  (aBpu)

We hope that these thoughts will stimulate some discussion and action within the broad audience affected. While the focus here is on the electrolytes, some other modifying symbols useful in POC will be the subject of further communications.

<sup>xvii</sup> For oxygen concentration, the dissolved plus the hemoglobin bound—each determined separately in the system, then added together is a ‘total’ oxygen formerly ‘oxygen content’. The latter term being appropriate for the 100-year-old technology from which it came. (9) I would eschew the use of ‘t’ alone for ‘total’ due to the potential confusion for time or temperature which could potentially be part of the same report.

**Bibliography/References:**

1. 1989 Burritt MF, Graham G, Burnett RW, et al. Standardization of Sodium and Potassium Ion-Selective Electrode Systems to the Flame Photometric Reference Method, Nat. Comm. Clin. Lab. Standards C29-P, Villanova, Penn., 1989.
2. 1990 Misiano DR, Moran RF, Effects of storage temperature on whole blood potassium measurements: implications in combined analysis of blood gases and electrolytes; In: Methodology and Clinical Applications of Electrochemical and Fiber Optic Sensors, 11, (Eds; Burritt MF, Moran RF), 231-238, AACC Electrolyte, Blood Gas Division, Rochester, MN, 1990
3. 1990 Moran RF, Misiano DR, Multi-channel analysis of electrolytes, blood gases and related analytes: implications of preanalytical treatment of samples, In: Methodology and Clinical Applications of Electrochemical and Fiber Optic Sensors, Volume 11, (Eds; Burritt MF, Moran RF), 197-219 AACC Electrolyte/Blood Gas Division, Rochester, MN.
4. 1991 Vanderlinde RE, Hertz HS, Bowers GN, et al., Development of certified reference materials for the National Reference System for the Clinical Laboratory, Nat Comm Clin Lab Standards NRSCL3-A, Villanova, Penn., 1991.
5. 1991 Vanderlinde RE, Hertz HS, Bowers GN, et al., Development of reference methods for the National Reference System for the Clinical Laboratory, Nat Comm Clin Lab Standards 1991 NRSCL2-A, Villanova, Penn., 1991.
6. 1992 Graham G, Bergkuist C, Burnett RW, Burritt MF, et al., Standardization of sodium and potassium, ion-selective electrode systems to the flame photometric reference method, Nat Comm Clin Lab Standards C29-T, Villanova, Penn., 1992
7. 1993 Moran RF, Implications for the intensivist in relating pre-analytical treatment of patient blood samples to clinical reliability of electrolytes, PCO<sub>2</sub> and total hemoglobin. West Pac Cong Crit Care Med, 1993
8. 1993 Moran, RF, Bergkuist C, Graham GA, Misiano DR, et al, Considerations in the simultaneous measurement of blood gases, electrolytes, and related analytes in whole blood-Proposed Guideline. Nat Comm Clin Lab Standards C32-P, Villanova, Penn., 1993
9. 1993 Moran R.F. Laboratory Assessment of Oxygenation J Int Fed. Clin. Chem. 5:4, 170-82
10. 1993 Moran Case for standardized terminology Crit Care Med, 21:5, 805-807.
11. 1995 D'Orazio P, Graham G, Bergkuist C, Cormier A, et al. Standardization of sodium and potassium ion-selective electrode systems to the flame photometric reference method - Approved Standard, NCCLS: C29-A, Villanova, Penn., 1995. (S37).
12. 1995 D'Orzaio P, Graham GA, Bergkuist C, Cormier AD, et al. Ionized calcium determinations: Pre-collection variables, specimen choice, collection, and handling - Approved Guideline NCCLS: C31-A, Wayne, Penn., 1995
13. 2001 Burnett R, Ehrmeyer SS, Moran RF, vanKessel A, Blood gas and pH analysis and related measurements; Approved Guideline. NCCLS C46-A, Wayne, PA, 2001.
14. 2017 Moran, RF, Podcast- Point of Care vs. Central Lab Discrepancies: Getting the message Across. JALM, 2017.
15. 2017 Moran, RF, Point of Care vs. Central Lab Discrepancies: Getting the message Across. JALM, 1:05, 595-597, 2017.
16. 2018 The ABC's of ABG's™: A Cyclopedic Dictionary of the Testing Terms Used in Critical Care; Momentum Press®, ISBN-13: 978-1-94708-348-6 (print); ISBN-13: 978-1-94708-349-3 (e-book).