AACB Draft Guidelines for
Harmonised Reporting of Arterial and Venous Blood Gas Result

Executive Summary

The AACB Blood Gases Harmonisation Working Party has drafted recommendations for harmonised arterial and venous blood gas reference intervals and for reporting blood gas results. This draft document is circulated for public comments before finalisation of the guideline.

Scope

Harmonisation for:
1. Arterial Blood Gas (ABG) and Venous Blood Gas (VBG) reference intervals
2. Tests: pH, pCO_2, pO_2, Bicarbonate (HCO_3), Lactate, Base excess (BE), Ionised calcium (iCa)
3. Population: Adults
4. Reporting: test names, units, LOINC codes, additional advice on reporting pH, ionised Ca, and base excess

Target group

This guideline aims to target laboratories that provide blood gas measurement service either in the laboratory or at the point of care.

Background and Methods

The prospect of harmonising Blood Gas Reference Intervals (RI) was first raised at the 2016 AACB Harmonisation workshop. Subsequent work was undertaken by NZ Point of Care Advisory Group (NZPOCTAG) and NSW Health Pathology (NSWHP) to determine ABG and VBG reference intervals, using various approaches that are detailed in the Methods section.

This draft recommendation is based on the collation of scientific evidence, statistical analysis of reference interval study data and data from multiple laboratories in Australia and New Zealand, as well as on the consensus of experts of the AACB guideline group, clinicians and the AACB Harmonisation Committee.

Key Recommendations for Harmonised Adult Blood Gas Reference Intervals

LOINC number	Measurand	Arterial Blood	Venous Blood
11558-4	pH	7.35 - 7.45	7.30 - 7.43
11556-8	pO_2	10.0 - 14.0 kPa* or 75 – 105 mmHg*	No RI
11557-6	pCO_2	4.7 - 6.0 kPa* or 35 – 45 mmHg*	5.1 - 7.7 kPa* or 38 – 58 mmHg*
1959-6	Bicarbonate	22 - 28 mmol/L	22 - 30 mmol/L
32693-4	Lactate	0.4 - 2.0 mmol/L	0.4 - 2.0 mmol/L
11555-0	Standard Base Excess	-3.0 to +3.0 mmol/L	-2.0 to +4.5 mmol/L
47596-2	Ionised Ca	1.15 - 1.30 mmol/L	1.15 - 1.30 mmol/L

* Both kPa and mmHg are acceptable units for reporting. In New Zealand kPa is the preferred unit, and in Australia mmHg is recommended for use. The data above represent the recommended decimal places for reporting each result.

Additional recommendations for reporting blood gas results:

- **Temperature corrected pH or pCO_2** should be reported without reference intervals. Cumulative results must be presented in separate lines for non-corrected and corrected results to enable appropriate clinical interpretation. For temperature corrected values the patient temperature must also be reported.
- Reporting **ionised calcium adjusted to pH 7.4 is discouraged**, as it is misleading in patients with abnormal acid-base status. If laboratories choose to adjust iCa to pH7.4 to correct for delay in sample processing and measurement it should only be reported on ABG and clearly distinguished from the actual measured ionised calcium result.
- **Standard Base Excess** rather than Actual Base Excess should be routinely reported in clinical practice.

Guideline

Methods

This draft recommendation is based on the following information gathered by the AACB guideline group:

- Surveys of ABG and VBG reference intervals used by laboratories in Australia and New Zealand.
- Review of published ABG and VBG reference interval studies.
- Review of reference intervals supplied by manufacturers of blood gas devices.
- Reference intervals for VBG established in a study of 134 healthy adults on Radiometer ABL 800 series analysers in NSW Health Pathology *(1)*.
- Meta-analysis of published differences between ABG and VBG results in hospitalised patients. This information was used for modelling theoretical VBG reference intervals from established ABG reference intervals and to compare those to the VBG RI study data *(1).*
- Bhattacharya analysis for establishing VBG reference intervals using a large dataset of patients (n=65,228) with a single VBG episode in an emergency hospital setting from ACT, NSW, NZ, VIC, QLD.
- Flagging rate analysis of proposed VBG reference intervals on the same large dataset obtained on various devices.
- Assessment of VBG RI transferability between Radiometer ABL 800 series, IL/Werfen GEM 4000 and 5000, and Abbott iStat platforms using patient comparisons (n=30-50) and the Royal College of Pathologists of Australasia Quality Assurance Program (RCPAQAP) end of cycle reports.
- Consultation with respiratory physicians and review of clinical guidelines on acute and chronic respiratory diseases *(2-5)*.

Outcomes of the above-mentioned investigations were presented at AACB Harmonisation meetings in 2018 and 2019. Expert consensus to use the proposed harmonised blood gas RI has been reached at the 2019 AACB Harmonisation meeting and after peer review and consultation with the following stakeholders:

- NSW Health Pathology
- NZ Point of Care Testing Advisory Group (NZPOCTAG)
- Auckland Region Quality Assurance Group (ARQAG)
- South Island Quality Assurance Group (SIQAG)
- 2019 AACB Harmonisation meeting participants
- AACB Harmonisation Steering Group

Results and rationale for recommendations

1. Reference intervals for ABG

The ABG RI reflect the state-of-the-art and have been established by expert consensus based on manufacturers' and published RI data and surveying the most frequently used RI in Australian and New Zealand laboratories. See recommendations in *Table 1.*

According to an RCPAQAP survey in 2018, the arterial pO_2 RIs were 80 – 100mmHg or 10.7-13.3 kPa; i.e. very close to the current recommendation. The hereby proposed arterial RIs for pH and pCO_2 were already the most commonly used RIs in this survey, suggesting that the recommended ABG RIs have been field tested and thus will not impose major changes for reporting ABG results in most laboratories.

Table 1: Recommendation for adult arterial blood gas reference intervals and reporting units based on the state-of-the-art and published sources

Measurand	Arterial
pH	**7.35 - 7.45**
pO_2	**10.0 - 14.0 kPa** **75 - 105 mmHg**
pCO_2	**4.7 - 6.0 kPa** **35 - 45 mmHg**
Bicarbonate	**22 - 28 mmol/L**
Lactate	**<2.0 mmol/L**
Standard Base Excess	**-3.0 to +3.0 mmol/L**
Ionised Ca	**1.15 - 1.30 mmol/L**

2. Reference intervals for VBG

2.1 For VBG, a **formal RI study** was carried out using samples of 134 healthy non-smoking adults on Radiometer ABL 800 series analysers in NSW Health Pathology *(1)*. The results are presented in *Table 2.*

2.2 The formal VBG RI study findings were compared to **theoretical VBG RI using meta-analysis data on published ABG-VBG differences** *(1)*, and **Bhattacharya analysis** on a large dataset of patients with a single VBG episode in an emergency care setting *(Table 2)*.

2.3 **Flagging rate analysis** of proposed VBG RI, presented at the 2018 AACB Harmonisation Workshop, was acceptable and similar across various blood gas devices *(Figure 1).*

2.4 Result **transferability analyses,** presented at the 2019 AACB Harmonisation Workshop, using data from RCPA QAP and patient sample comparisons, indicate harmonisation of RI is possible for pH, pCO_2, HCO_3, lactate, and ionised calcium *(Figure 2).*

Table 2: Adult venous blood gas reference intervals using various approaches

Measurand	*Units*	*Reference interval study (1) (2.5-97.5 centile)*	*Theoretical VBG RI modelled using ABG-VBG differences (1)*	*Bhattacharya analysis of 65,228 single ED patient episodes*	*Clinical consultation and expert consensus*
pH		7.30 – 7.43	7.32 – 7.42	7.30 – 7.48	7.30 – 7.43
pO_2	mmHg	19 – 65	44 – 69	NA	Not recommended
	kPa	2.5 – 8.7	5.9 – 9.2		Not recommended
pCO_2	mmHg	38 – 58	36 – 52	29 – 56	38 – 58*
	kPa	5.1 – 7.7	4.8 – 6.9	3.9 – 7.5	5.1 – 7.7*
Bicarbonate	mmol/L	22 – 30	23 – 27	19 – 31	22 – 30
Lactate	mmol/L	0.4 – 2.2	0.8 – 1.9	NA	0.4 – 2.0
Standard Base Excess	mmol/L	-1.9 – 4.5	NA	NA	NA
Ionised Calcium	mmol/L	1.14– 1.29	NA	1.08 – 1.29 **	1.15 – 1.30

* Venous pCO_2 decision limit for ruling in type2 respiratory failure in the right clinical context is >50mmHg >6.7 kPa) based on clinical consensus (see notes under 2.5.c below)

**Ionised calcium reference interval 1.14 – 1.33 mmol/L, when adjusted to healthy mean venous pH of 7.365

2.5. Recommendations for adult venous blood gas reference intervals and reporting

The below recommendations are based on experimental data and analysis mentioned above under points 2.1-2.4 and consultation and consensus with respiratory physicians and laboratory professionals.

a. **pH**: Use the NSWHP VBG RI study data *(1)* for pH (i.e. 7.30 – 7.43) and do not round up these figures for ease of use.

b. **pO_2**: Do not provide pO_2 results and RI on VBG samples. If pO_2 testing is required, measurement of ABG should be recommended to appropriately assess oxygenation *(1)*.

c. **pCO_2**: We recommend using the NSWHP VBG RI study data (i.e. 38-58 mmHg or 5.1-7.7 kPa *[1]*) until better evidence emerges for the use of clinical decision limits (see Note below).

Note: Respiratory physicians prefer using a decision limit rather than an upper reference limit for pCO_2 when managing Type 2 respiratory failure *(2-6)*. The more conservative venous pCO_2 decision limit of >50 mmHg (6.7 kPa) reflects the venous equivalent of an arterial pCO_2 threshold (i.e. >45 mmHg or >6.0 kPa) that most respiratory guidelines use for the diagnosis of type 2 respiratory failure *(3-6).* McCanny et al. propose an even lower decision threshold and claim that a cut-off of venous pCO_2 of >45 mmHg is 100% sensitive in predicting arterial hypercapnia in acute exacerbation of chronic obstructive pulmonary disease *(6)*. This recommendation will be updated when an ongoing Cochrane systematic review provides firmer evidence for the use of decision limits for VBG pCO_2 in type 2 respiratory failure *(7).*

d. **Bicarbonate:** We recommend using the NSWHP VBG RI study data (i.e. 22-30 mmol/L *[1]*).

e. **Lactate**: For VBG lactate we recommend using the same reference limit as for ABG, even though lactate is slightly higher in venous than arterial blood (e.g. the upper reference limit [URL] in the NSWHP VBG RI study was 2.2 mmol/L, *versus* an ABG URL of 2.0 mmol/L). Given the biological and analytical variation of lactate and the known preanalytical factors during phlebotomy, the use of the same RI for ABG and VBG is scientifically acceptable and pragmatic. To avoid using 'less than' signs, which most IT systems cannot handle well and clinicians may misread, we propose the lower reference limit established in the VBG study (i.e. 0.4 mmol/L) to be used for both ABG and VBG lactate.

f. **Standard Base Excess:** We recommend using the NSWHP VBG RI study data (i.e. -2.0 to 4.5 mmol/L *[1]*).

g. **Ionised Ca:** For VBG and ABG ionised Ca (iCa), laboratories can decide to use the same reference limits, if preanalytical factors can be controlled during phlebotomy (Note: the NSWHP VBG RI study limits are 1.14 – 1.29 mmol/L *(1)*; very close to the ABG reference limits of 1.15-1.30 mmol/L).

However, Bhattacharya analysis has resulted in a lower reference limit for iCa and a higher upper reference limit for pH than in the formal VBG RI study *(Table 2)*. The higher pH could explain the lower iCa results observed in a large routine dataset. When this dataset was corrected for the mean VBG pH of 7.365, results were more in line with the findings of the RI study *(Table 2).*

Whether these findings are due to the spectrum of patients in emergency (stress, anxiety, hyperventilation associated with higher pH, and resultant lower iCa) or to preanalytical issues during phlebotomy, is unknown. Local verification of the proposed RI may be required, especially if the rate of preanalytical problems is relatively high and difficult to control.

3. Additional considerations for reporting blood gas results

Reporting units

The New Zealand Group proposed harmonisation of reporting pO_2 and pCO_2 to SI units, however, unit changes would require a much broader consensus with clinicians, revision of any relevant clinical guidelines, instrumentation and a major awareness campaign. Units for pO_2 and pCO_2 remain different in New Zealand. The guideline group has consulted with the RCPA PITUS working party on standardisation of terminology and units in pathology which accepts both mmHg and kPa as reporting units for these two measurands *(8)*.

Temperature corrected pH or pCO_2

In certain clinical circumstances associated with hyperthermia or hypothermia during an acute or critical illness or surgery, laboratories may be requested to report temperature corrected blood gas results. Some blood gas analysers are able to report temperature corrected results after inputting the patient's actual temperature, and these corrected results reflect the true *in vivo* values of a hypo/hyperthermic patient. There is no clear evidence on the clinical value of temperature correction of blood gas results in terms of patient outcomes *(9)*.

If laboratories offer temperature corrected blood gas results:

a) the non-corrected blood gas results should always be reported together with the harmonized reference intervals;
b) temperature corrected blood gas results should be clearly labelled with an appropriate test name that distinguishes the result from the non-corrected result e.g., temperature corrected pH, or temperature corrected pCO_2.
c) In lack of published reference limits, temperature corrected pH or pCO_2 should be reported without reference intervals.
d) Cumulative results must be presented in separate lines for non-corrected and corrected results to enable appropriate clinical interpretation.
e) The temperature of the patient at the time of sampling should be included in the report.

Ionised Ca adjusted to pH

The pH adjustment is based on CO_2 loss from a sample in the pre-analytical phase, and should not be reported on correctly sampled blood gas samples *(10)*.

Ionised calcium measurements should not be adjusted to the average of arterial pH of 7.40 when the actual pH measurement accurately reflects the patient's acid-base status. Adjusting the ionised calcium to 'standardised' arterial pH in this case will hide the physiological drop in ionised calcium in alkalosis or the rise of ionised calcium in acidosis. Adjustment of ionised Ca in venous blood (which physiologically has a lower average pH of 7.365) to the average pH of arterial blood (i.e. pH 7.40) is inappropriate.

Some laboratories in certain cases adjust ionised calcium in blood to arterial pH 7.40 to eliminate an obvious preanalytical error due to delayed sample transport or inappropriate sample handling before analysis that results in a loss of CO_2 in the specimen. Such adjustment assumes that the patient's true pH was 7.40 before the sample has deteriorated.

We discourage reporting ionised calcium adjusted to arterial pH 7.40 in both arterial and venous blood gas samples, as it is misleading in patients with abnormal acid-base status *(10)*.

Base Excess

Base Excess (BE) is a clinically useful parameter and provides a measure of any metabolic contribution to an acid-base disturbance. Most blood gas analysers offer the option of calculating either the base excess of the blood sample (Actual Base Excess) or the base excess of the extracellular fluid (Standard Base Excess).

Standard Base Excess is reported as part of blood gas analysis and is often used as a measure of non-respiratory acid-base disturbance. However, the Base Excess calculated for the *in vitro* specimen (Actual BE) may not represent the *in vivo* situation. This is because in the whole body the acid-base changes occurring in the vascular compartment (red cells and plasma) also involve buffer shifts across the extra and intra-cellular compartments. Thus, acute changes of pCO_2 *in vivo* cause HCO_3- shifts between blood and the extracellular fluid, and therefore the Actual Base Excess calculation is not independent of pCO_2. Thus reporting Actual Base Excess has the potential for clinical misinterpretation, particularly in patients with severe hypercapnia, in whom there may be an incorrect suggestion of a metabolic component to the disturbance *(11)*.

It is therefore recommended that Standard Base Excess (SBE; a.k.a. cBase[ecf]) be routinely reported in clinical practice which assumes an extracellular fluid (ecf) haemoglobin concentration of 50 g/L. Venous SBE is approximately 1 mmol/L higher than in arterial blood due to the Haldane effect as venous blood deoxy-haemoglobin is a weaker acid than oxy-haemoglobin in arterial blood *(12)*.

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NSW Health Pathology: Amanda Caswell

VBG Reference Intervals Subgroup
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Westmead Children's Hospital: Jason Chung

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ACT Pathology: David Hughes
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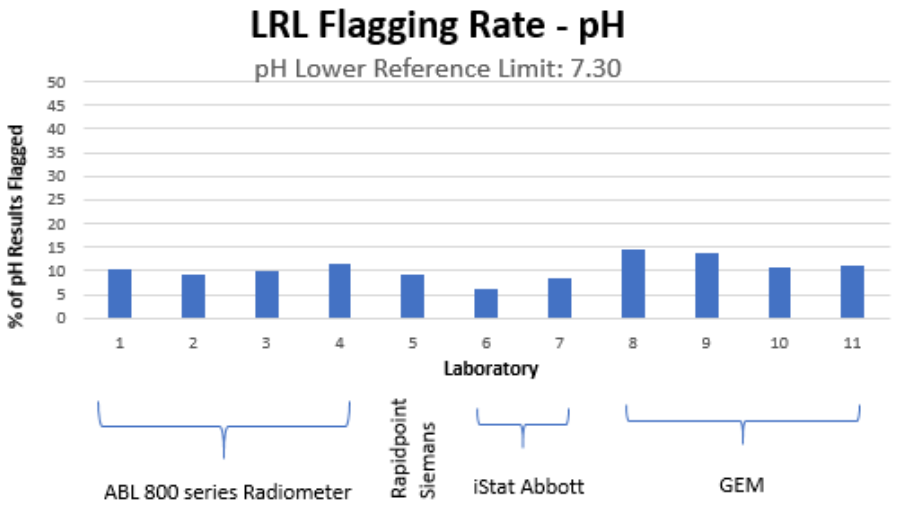
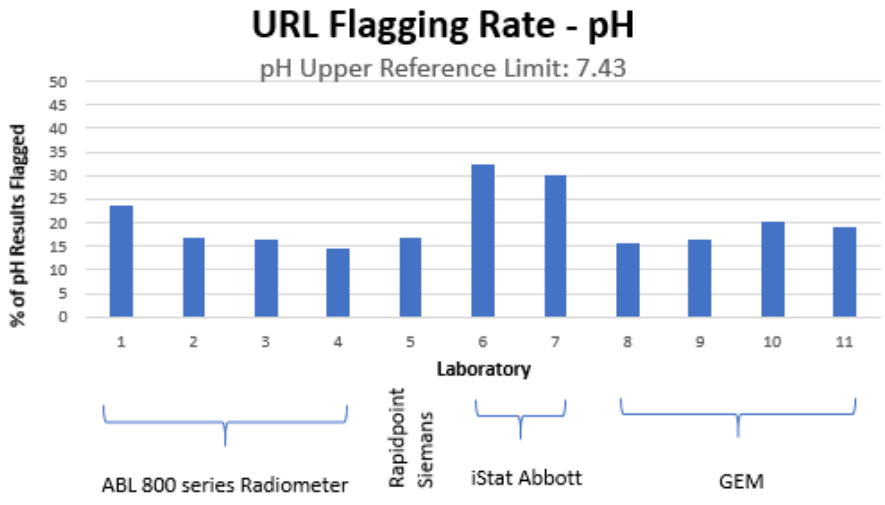
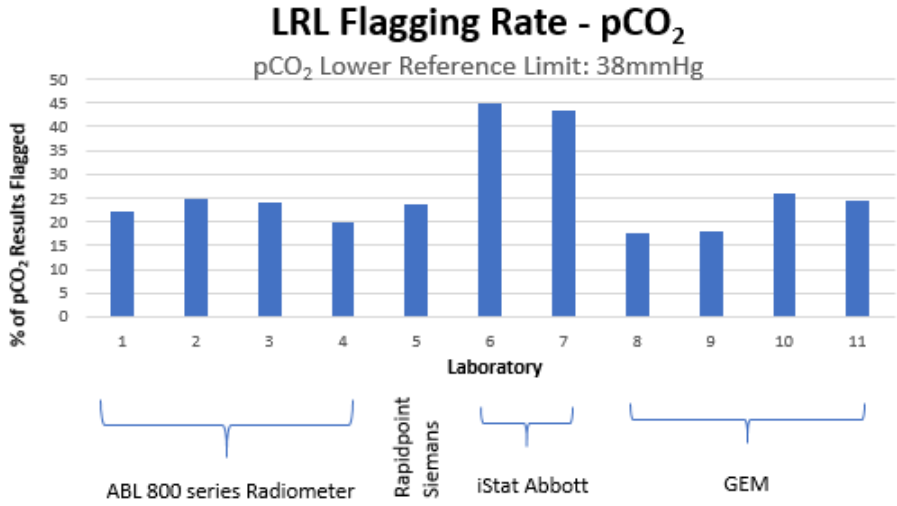
Michael Peake, Grahame White

Figure 1: Flagging rate analysis of proposed venous blood gas reference intervals.

N=**65,228 single patient episodes in emergency department settings**







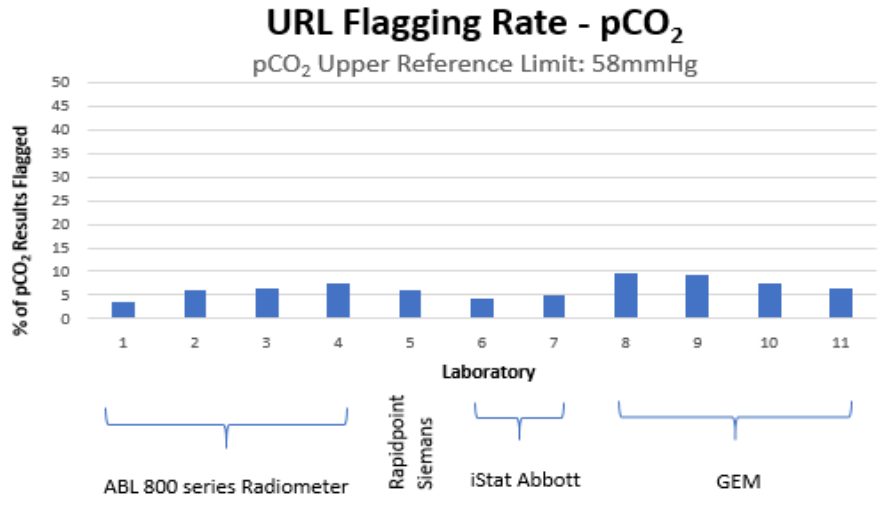
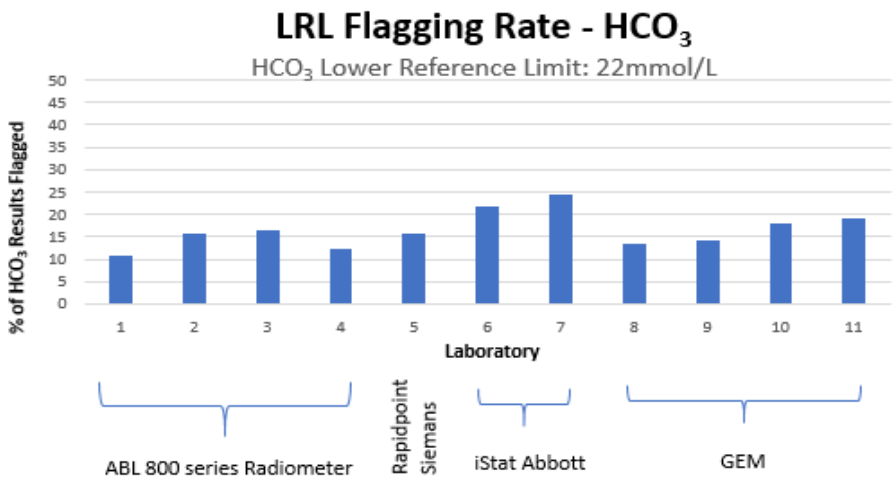
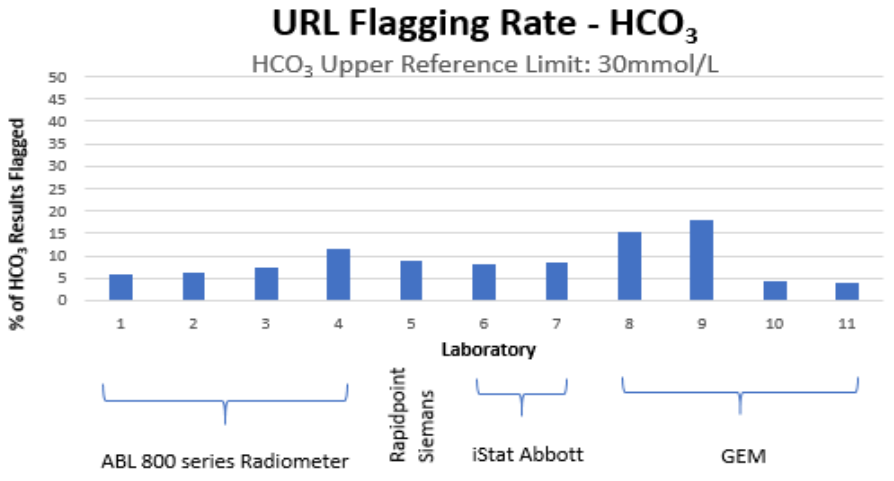
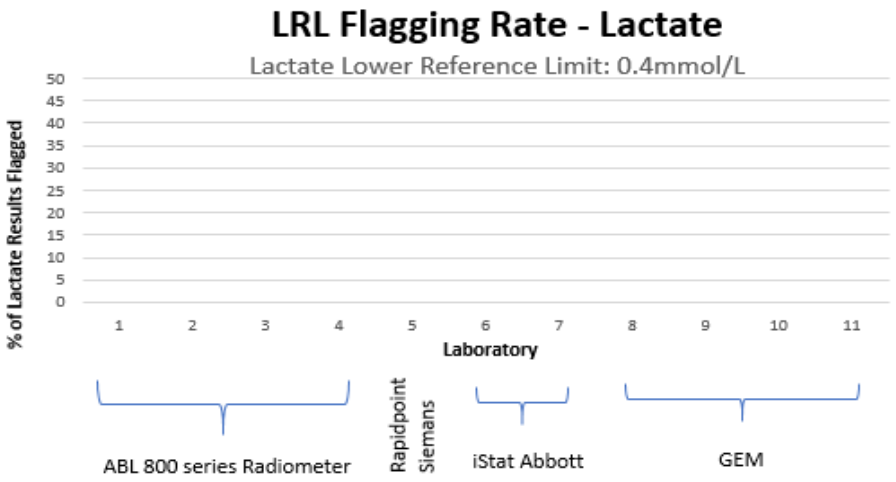


Figure 1 continued: Flagging rate analysis of proposed venous blood gas reference intervals.

N=**65,228 single patient episodes in emergency department settings**







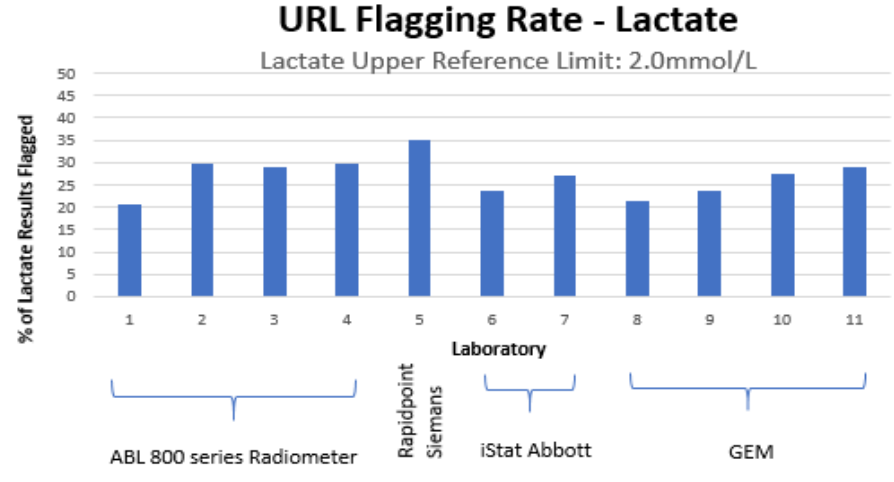
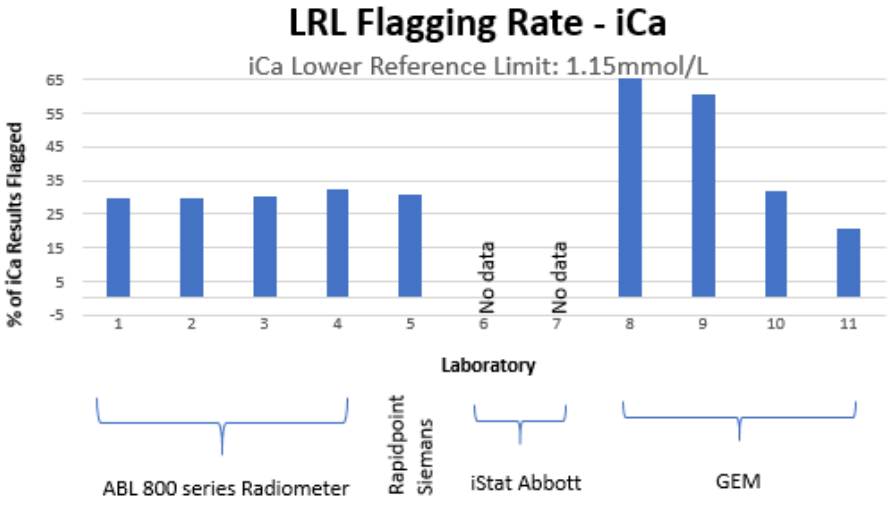


Figure 1 continued: Flagging rate analysis of proposed venous blood gas reference intervals.

N=**65,228 single patient episodes in emergency department settings**



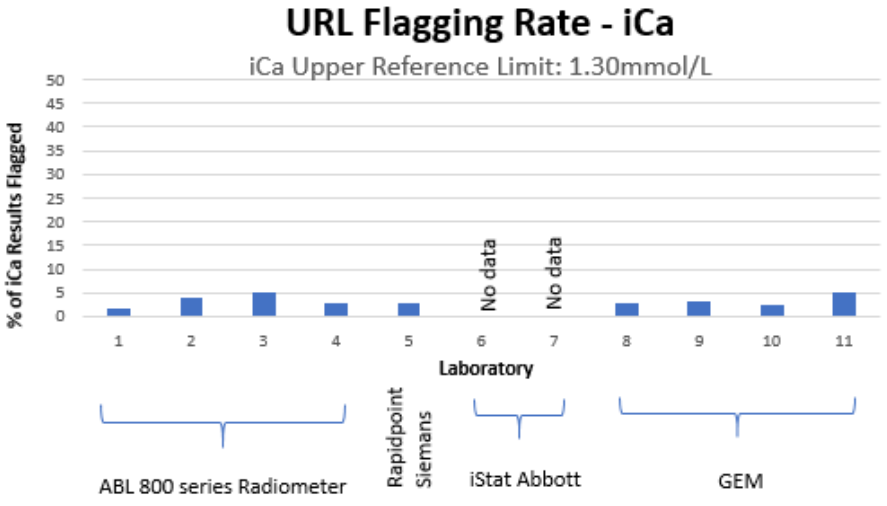
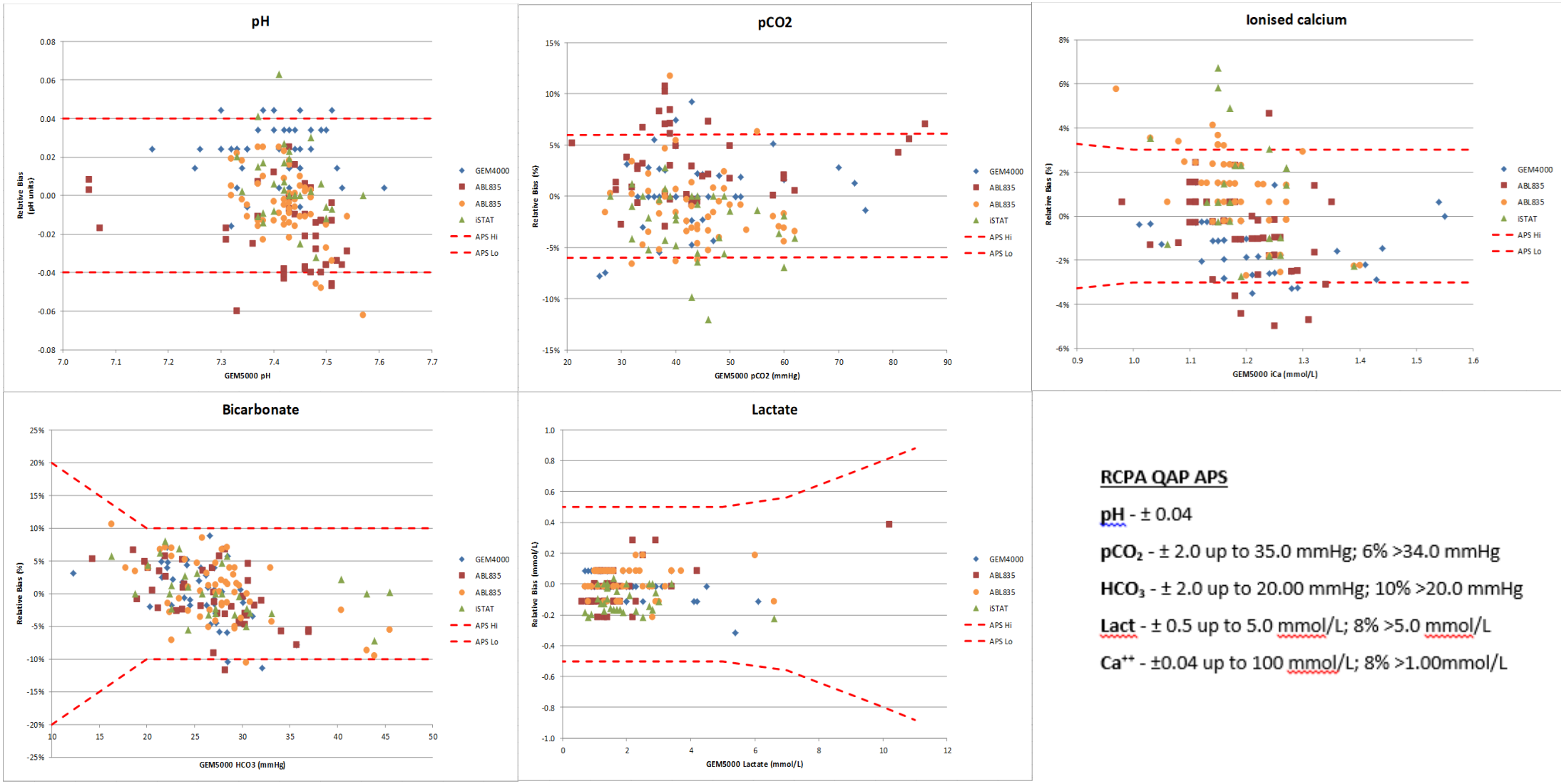


Figure 2: Transferability of venous blood gas reference intervals between methods

Relative bias between GEM5000 vs GEM4000, two ABL835 and iSTAT devices



RCPA QAP APS

pH - ± 0.04

pCO_2 - ± 2.0 up to 35.0 mmHg; 6% >34.0 mmHg

HCO_3 - ± 2.0 up to 20.00 mmHg; 10% >20.0 mmHg

Lact - ± 0.5 up to 5.0 mmol/L; 8% >5.0 mmol/L

Ca^{++} - ±0.04 up to 100 mmol/L; 8% >1.00mmol/L