Competitive Evaluation of the GEM® Premier™ 3000 with Intelligent Quality Management (iQM™).

P. D'Orazio, PhD and H. Visnick*

The performance of the GEM Premier 3000 with iQM was compared to the following competitive systems: Bayer Rapidlab® 855, Bayer Rapidpoint® 405, Nova pHOx® plus L, and Radiometer ABL™77. The systems were compared for accuracy using available reference materials and methods, and for the response of the systems to blood samples containing interfering substances and clots.

This study shows the GEM Premier 3000 to have clinically acceptable accuracy when evaluated using available reference materials and methods for PO_2, PCO_2, Na^+, K^+, Ca^{++} glucose and hematocrit. Overall, the GEM Premier 3000 demonstrated superior accuracy to the competitive systems for measurement of these analytes. iQM was shown effective in flagging the presence of interfering substances in samples and the presence of blood clots on sensors. In all cases, interfering substances were flagged by iQM, while in some cases the competitive systems reported unflagged, erroneous results. The clot-detection and clearing mechanisms of iQM make the GEM Premier 3000 superior to the competitive systems for handling problems created by the presence of blood clots in samples.

Introduction

The performance of the GEM Premier 3000 with iQM was compared to the following competitive systems:

- Bayer Rapidlab 855
- Bayer Rapidpoint 405
- Nova pHOx plus L
- Radiometer ABL 77

The systems were compared for the following:

1. Accuracy using available reference materials and methods:
   - Na^+, K^+, Ca^{++}: SRM 956a from the National Institute for Standards and Technology (NIST) (certified reference material)
   - glucose: SRM 965 from NIST (certified reference material)
   - PCO_2, PO_2: whole blood tonometry (reference method)
   - hematocrit: microcentrifugation (reference method)

   Accuracy for measurement of pH and lactate was not conducted due to unavailability of reference methodology or serum-based reference materials for these analytes.

2. Interference produced by two substances known to interfere with electrode-based critical care systems: benzalkonium and thiopental, representing a macromolecular cation and anion, respectively.

3. Problems produced by introduction of clots to the systems and evaluation of clot-handling mechanisms of the systems.

*Instrumention Laboratory, Lexington, MA

Materials and Methods

All instruments were set up and maintained according to the manufacturer's instructions. Table 1 is a summary of the analytes available and the quality control system for each instrument. Each instrument was required to pass its own quality control prior to beginning the evaluation.

Table 1
Analytes and Quality Control Systems for the GEM Premier 3000 and Competitive Instruments

System	Available Analytes	Quality Control System
GEM Premier 3000	pH, PCO_2, PO_2, Na^+, K^+, Ca^{++}, glucose, lactate, Hct	iQM
Rapidlab 855	pH, PCO_2, PO_2, Na^+, K^+, Ca^{++}, Cl^-, CO-Oximetry*	three-level ampouled QC material
Rapidpoint 405	pH, PCO_2, PO_2, Na^+, K^+, Ca^{++}, Cl^- glucose, CO-Oximetry	On-board auto QC module
pHOx plus L	pH, PCO_2, PO_2, Na^+, K^+, Cl^- (or Ca^{++}), glucose, lactate, SO_2%, Hct, Hb	On-board auto QC pack
ABL 77	pH, PCO_2, PO_2, Na^+, K^+, Ca^{++}, Cl^-, Hct	four-level ampouled QC material

*Evaluation of CO-Oximetry performance not included in this test.

Accuracy

SRM 956a and SRM 965a were obtained from NIST and prepared according to the manufacturer's instructions. SRM 956a is a frozen human-serum-based reference material with certified concentrations for Na^+ and K^+ and reference concentrations for Ca^{++} at three different levels. SRM 965a is a serum-based reference material for glucose at four different certified concentrations. Each material was assayed in duplicate on each system and results compared to values given on the certificates of analysis. Whole blood tonometry was performed at four different levels of PCO_2 and PO_2. Each sample was assayed in duplicate on all the systems and the measured concentration compared to the expected value. Whole blood was adjusted to five different levels of hematocrit by removing plasma or diluting with either plasma or Plasma-Lyte A (Baxter). Each sample was assayed in duplicate on all the systems and the measured hematocrit compared to the value obtained by microcentrifugation.

In all cases, bias versus the expected result was compared against clinically acceptable error, based on CLIA 88 limits.

Table 2
Concentrations of Electrolytes and Glucose in NIST SRM 956a and SRM 965a

	SRM 956a			SRM 965a
	Na^+ (mmol/L)	K^+ (mmol/L)	Ca^{++} (mmol/L)	Glucose (mg/dL)
Level 1	121.4	6.008	1.741	34.56
Level 2	141.0	3.985	1.411	78.50
Level 3	160.9	2.025	1.091	122.1
Level 4				292.6

Interfering Substances

Benzalkonium chloride was spiked into whole blood at concentrations of 5 and 10 μg/mL. Sodium thiopental was spiked into whole blood at concentrations of 30 and 50 μg/mL. Samples were run on all the systems and results compared to unspiked blood to determine the amount of interference, which was further compared against clinically acceptable error, based on CLIA 88 limits.

Clots

Clots were formed by addition of thrombogenic compounds, RecombiPlasTin[i] and SynthASil®[ii] (Instrumentation Laboratory), to whole blood. Blood samples containing clots were introduced to the systems and any resulting errors were noted. Quality control materials for each system were run following exposure to blood samples containing clots to test for any effects on the sensors, except for the GEM Premier 3000 where this function is handled automatically by iQM.

Results

Accuracy

Figures 1 and 2 show the whole blood tonometry results for PO_2 and PCO_2, respectively. Figures 3-6 show the recovery versus expected concentrations for Na^+, K^+, Ca^{++}, and glucose, respectively. Figure 7 shows the whole blood hematocrit results. The data are plotted as the result given by each test instrument minus the expected value. Bias versus the expected result is compared against clinically acceptable error based on CLI A 88 limits.

K^+ results for the Nova pHOx plus are not shown due to repeated electrode failures and inability to maintain the channel operational.

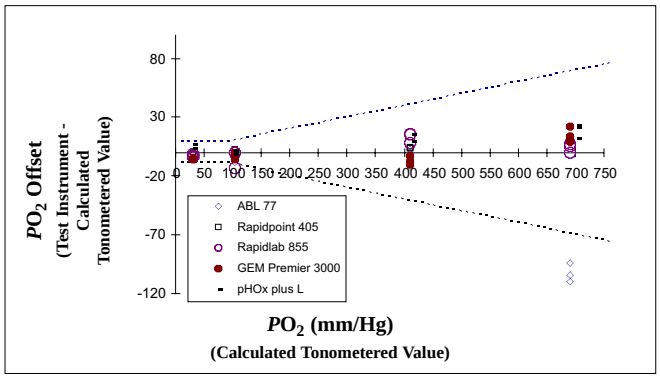

Figure 1
PO_2 Accuracy in Competitive and GEM Premier 3000 Instruments
Test Instrument - Expected Tonometered Value

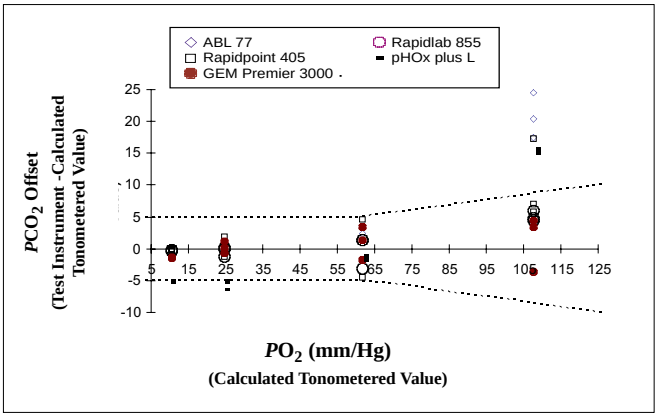

Figure 2
PCO_2 Accuracy in Competitive and GEM Premier 3000 Instruments
Test Instrument - Expected Tonometered Value

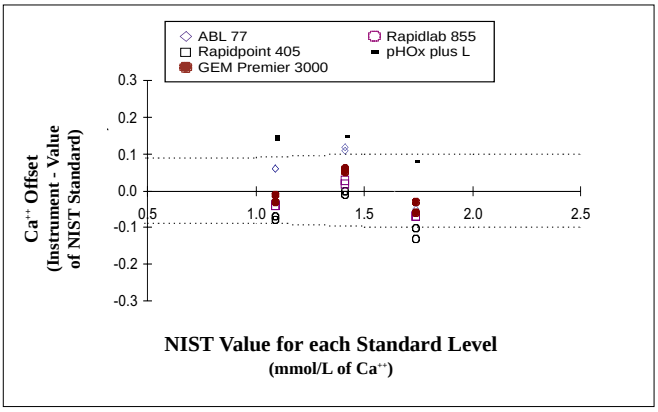

Figure 5
Ca^{++} Accuracy Using NIST Standards in Competitive and GEM Premier 3000 Instruments
Instrument Values - NIST Reference Values

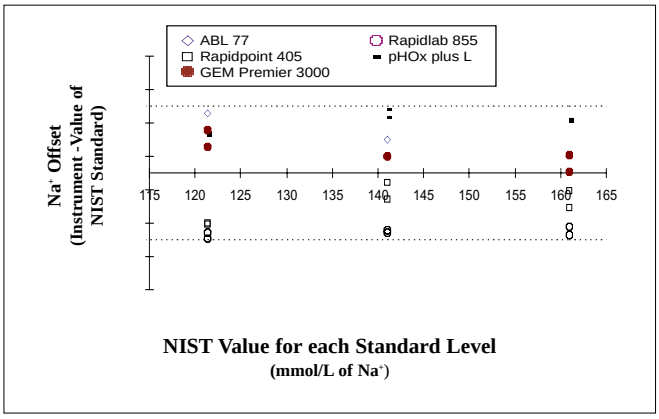

Figure 3
Na^+ Accuracy Using NIST Standards in Competitive and GEM Premier 3000 Instruments
Instrument Values - NIST-Certified Values

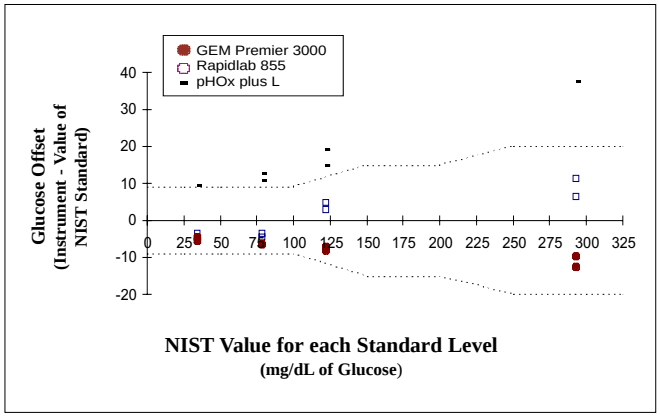

Figure 6
Glucose Accuracy Using NIST Standards in Competitive and GEM Premier 3000 Instruments
Instrument Values - NIST-Certified Values

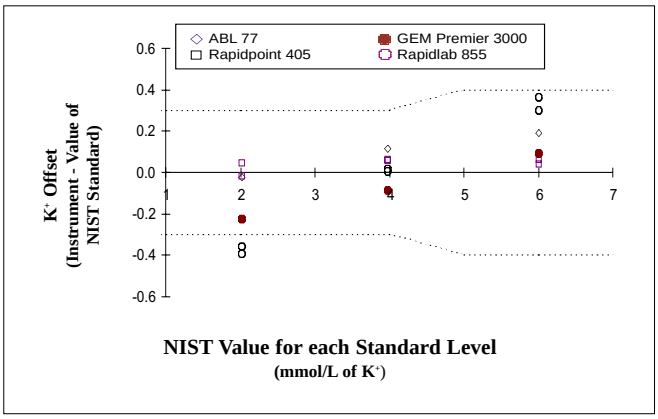

Figure 4
K^+ Accuracy Using NIST Standards in Competitive and GEM Premier 3000 Instruments
Instrument Values - NIST-Certified Values

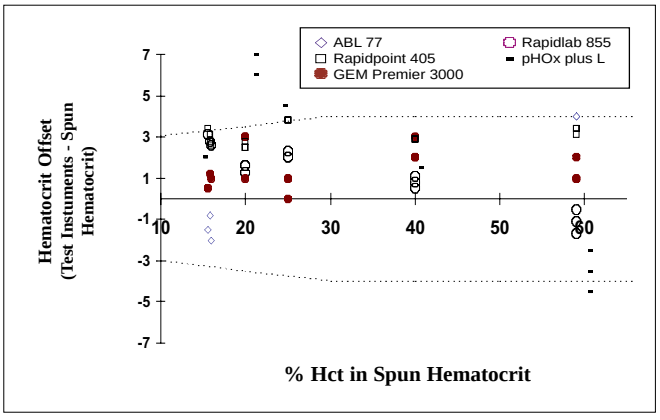

Figure 7
Hematocrit Accuracy of Blood in Competitive and GEM Premier 3000 Instruments
Instrument Values - Spun Hematocrit

Interfering Substances

Table 3 below shows the amount of interference by benzalkonium and thiopental on the GEM Premier 3000 and competitive systems for the following analytes: pH, PCO_2, Na^+, Ca^{++} and PO_2. Other analytes were not affected by the presence of these substances in any of the systems. Shaded areas show where the interference, expressed as the delta in the reported value due to the interfering substance, exceeded the clinically acceptable level or other problems were detected.

Table 3
Effect of Benzalkonium and Thiopental on the GEM Premier 3000 and Competitive Instruments

Interfering Substance Spiked into Whole Blood	GEM Premier 3000*	ABL 77	pHOx plus L	Rapidpoint 405	Rapidlab 855
Benzalkonium (5ug/mL)					
- pH	-0.03, -0.02	-0.02, 0	-0.033	-0.005	-0.038
- PCO_2 (mmHg)	-1, 2	0, -1.5	5.5	-4.3	2.6
- Na^+ (mmol/L)	2,3	2.5, 2.5	-3.4	off scale ↑	-9.3
- Ca^{++} (mmol/L)	0.30, 0.20	0.03	-0.02	0.05	0.09
- PO_2 (mmHg)	0, -4.5	0, 3	-0.1	0.7	2.6, 4.9
Benzalkonium (10 ug/mL)					
- pH	-0.04	0	-0.037	-0.053	-0.019
- PCO_2	1	-0.5	3.9	did not read	-0.2
- Na^+	5	5	-7.8	off scale ↑	-0.5
- Ca^{++}	0.36	-0.02	0.01	0.04	0.03
- PO_2	-5.5	4	-0.7	-4.8	did not read
Thiopental (30 ug/mL)					
- pH	-0.01	0	-0.007	-0.002	0.01
- PO_2	34	0	0.5	6.4	-1.1
- Na^+	-2	0	-0.7	-1.1	-2.1
- Ca^{++}	-0.21	-0.02	-0.01	-0.03	-0.04
- PO_2	-1	0	-2.2	2.4	0.9
Thiopental (50 ug/mL)					
- pH	0.01	0.01	-0.005	0.012	-0.001
- PCO_2	5	-3	-0.1	1.6	0
- Na^+	5	1	-0.1	1.6	0.2
- Ca^{++}	-0.41	-0.01	-0.03	-0.03	-0.01
- PO_2	-1	0	-2.1	3.1	1.7
Allowable error					
- pH	± 0.04				
- PCO_2	± 5				
- Na^+	± 4				
- Ca^{++}	± 0.1				
- PO_2	± 10%				

* Interference for the GEM Premier 3000 detected by iQM in all cases.

Clots

ABL 77

A total of nine samples containing clots were introduced into the ABL 77 with the following results.

- Clots produced "???" on the results screen with "air in sample" message.
- Following a clot being trapped in the sensor channel, incorrect values were reported for whole blood samples which followed, but the system did not flag them as such. Example:

	pH	PCO_2	PO_2	Na^+	K^+	Ca^{++}	Cl^-	Hct
Expected values	7.19	64	44	131	7.7	1.28	107	40
Values reported with clots in sensor channel	7.46	28	187	122	1.1	0.5	82	---
Bias vs. expected value:	**0.27**	**-56%**	**325%**	**-7%**	**-86%**	**-61%**	**-24%**	

- QC samples were run while a clot was trapped in the sensor cassette. In one case, the QC result was so errant for pH that the sample was identified as the wrong level of QC, and could have been accepted as such.
- When a clot was trapped in the sensor cassette, if the operator observed the sample path, it was obvious that sample was not flowing normally. However, it was not until the next two-point calibration was initiated that the instrument flagged a problem ("sensitivity below minimum range") and no further samples would be accepted.
- Clots were cleared out of the sensor cassette with great difficulty (forcing air and liquid in and out of the sensor cassette with a syringe). Normal system washes would not remove clots from the sensor cassette.

Rapidlab 855

A total of 10 samples containing clots were introduced into the Rapidlab 855 with the following results.

- A blood sample containing a clot was rejected by the analyzer due to "bubbles detected in sample", and no sample results were reported.
- A clot became trapped in the sample introduction area and an obstruction message appeared. The sample was not aspirated and no results reported. A user-initiated wash was needed to clear the obstruction.
- A clot entered the CO-Ox sample path and was very difficult to remove. The CO-Ox stopped functioning after that event requiring a service call to correct the problem.

Rapidpoint 405

A total of ten samples containing clots were introduced into the Rapidpoint 405 with the following results.

- The clot-catcher stopped one clot. No sample was aspirated into the system and the sampling was aborted.
- Another clot was stopped by the clot-catcher, but evidently a small piece of the clot passed through the probe and became trapped in the internal fluidics of the cartridge. The instrument requested that the cartridge be removed and discarded.
- Another small clot was aspirated into the system. The analyzer determined that there was a problem with the sample because certain analytes were not reported (appeared with "X" over the analyte symbol). It took 17 minutes for all sensors to start reporting again.

- When a clot was stopped by the clot-catcher, the clot-catcher needed replacement. This was a tedious procedure, requiring approximately ten minutes.

pHOx plus L
A total of ten samples containing clots were introduced into the pHOx plus L with the following results.

- Clots produced fluidic problems flagged as "insufficient sample", "sample flow" and "std A flow" errors, with instructions to check the flow path and prime the standards. After repeated attempts to introduce clots with resulting fluidic errors, the system would not accept any more samples. Tubing had to be removed and flushed.
- After the clots were removed and the system was recalibrated, controls were run. For an unknown reason, the pH, Na^+, K^+, Ca^{++} and Hct channels did not report any results for three samples after the clot was cleared.

GEM Premier 3000 with iQM
A total of 21 samples containing clots were introduced into the GEM Premier 3000 with the following results.

- For six out of 21 samples, the narrow inlet probe did not allow clots to enter the system. Error messages 1.06 ("no sample solution detected") and 1.07 ("no air before sample solution detected") were the most frequent messages. The clots were trapped in the tip of the inlet probe and automatically wiped off by the probe wiper. In every instance, the analyzer was ready to accept another sample after automatically wiping off the clot.
- For three samples, a clot did enter the system and was trapped on a sensor triggering an iQM "clot pattern detected". All three clots were immediately cleared by the iQM corrective action. No sensors were disabled due to clots during this study.
- The 12 remaining samples were analyzed without problem, indicating that clots were not trapped on any sensors.

Conclusions

Accuracy
Accuracy for measurement of blood gases, electrolytes, glucose and hematocrit on the GEM Premier 3000 with iQM was acceptable at all levels.

The competitive systems showed a variety of problems with accuracy, based on the accuracy limits applied in this study.

pHOx plus L:
- High bias for PCO_2 at the high end of the range (>100 mmHg)
- High bias for Ca^{++} at the normal and mid concentrations.
- High bias for glucose at all four levels
- High bias at the low end of the range and low bias at the high end of the range for hematocrit

ABL 77:
- Low bias for PO_2 at the high end of the range (700 mmHg)
- High bias for PCO_2 at the high end of the range (>100 mmHg)
- High bias for Ca^{++} at the mid-level

Rapidpoint 405:
- High bias for PCO_2 at the high end of the range (>100 mmHg)

Rapidlab 855:
- Low bias for K^+ at the low end of the range
- Low bias for Ca^{++} at the high end of the range

Interfering Substances
All the systems evaluated showed some degree of interference from benzalkonium and thiopental. The advantage of the GEM Premier 3000 was that in all cases, the presence of an interfering substance was flagged by iQM. With the competitive systems, in some cases, erroneous result were reported without the flagging of an error. See Table 3.

Clots
Clots which were introduced into the competitive systems produced mainly various fluidic errors which were more of an inconvenience, resulting in down-time and maintenance, than a risk of reporting incorrect results. The exception was the ABL 77, where incorrect blood results were reported, with no flags present, when clots were present in the sensor cassette. See Results Section.

Overall, clots were handled best by the GEM Premier 3000 with iQM where the sample probe inlet stopped the clots before they could disable the fluidics. Clots on the probe were cleared by the system, avoiding the inconvenience of removing and replacing or cleaning a clot-catcher. Clots that were able to pass through the probe were handled by iQM clot detection, clearing and re-enabling new features of GEM Premier 3000 software.

A total of 21 samples containing clots were produced in this evaluation. Owing to the efficiency of the GEM Premier 3000 with iQM to in handle clots, it was possible to introduce all 21 samples to the system. However, only about half of the total samples (nine-ten) could be applied to the competitive systems. This was due to instrument down-time, resulting mainly from fluidic errors, created by the clots. These fluidic errors required user intervention (e.g., initiated washes and calibrations, replacing or cleaning clot-catchers, removal and flushing of tubing) during which samples could not be analyzed.

In summary, this study demonstrates that the GEM Premier 3000 with iQM has clinically acceptable accuracy when evaluated using available reference materials and methods for PO_2, PCO_2, Na^+, K^+, Ca^{++}, glucose and hematocrit. Overall, the GEM Premier 3000 with iQM delivered superior accuracy to the competitive systems for measurement of these analytes.

iQM was shown effective in flagging the presence of interfering substances in samples and the presence of blood clots on sensors. In all cases, interfering substances were flagged by iQM, while the competitive systems reported unflagged, erroneous results in some instances. The clot-detection and clearing mechanism of iQM in GEM Premier 3000 software, together with the narrow inlet of the sample probe, make the GEM Premier 3000 with iQM superior to the competitive systems, particularly for handling problems created by the presence of blood clots in samples.

[i]HemosIL RecombiPlasTin is a human recombinant tissue factor reagent for Prothrombin Time (PT) testing.

[ii]HemosIL SynthASil is a synthetic phospholipid-based reagent for Activated Partial Prothrombin Time (APTT) testing.