Comparison of the Sysmex XE-2100 to the Abbott Cell-Dyn 4000, Automated Hematology Analyzer

Cindy UPTMORE, MT(ASCP), CLS(NCA)*[1], Barbara CONNELL, MS, MT (ASCP), SH*[1]
David HART, MT(ASCP) *[2], and David S. HELMS, MT(ASCP) *[2]

*[1] *Sysmex Corporation of America, One Wildlife Way, Long Grove, IL 60047-9596, USA.*
*[2] *Clarian Health Partners, Department of Pathology and Laboratory Medicine, Division of Hematopathology, lndianapolis, IN, USA.*

The Sysmex XE-2100 automated hematology analyzer was evaluated at Clarian Health Partners (CHP), Indianapolis, IN. Results from 251 patient samples were compared to the Abbott Cell-Dyn 4000 (CD-4000). The XE-2100 showed good correlation with the results to the CD-4000 for the following parameters: white blood cell (WBC), neutrophil (NEUT) %, lymphocyte (LYMPH) %, monocyte (MONO) %, eosinophil (EO) %, basophil (BASO) %, red blood cell (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), reticulocyte (RET)%, impedance platelet (PLT-I), optical platelet (PLT-O). Sensitivity studies performed for the overall flagging capabilities showed the XE-2100 to have significantly lower false negatives (FN) than the CD-4000, although CD-4000 had a lower false positive (FP) rate. In this study we also looked at what adjustments to the Q-flags on the XE would do to the flagging. We found that lower FN and lower FP than the CD-4000 could be obtained on the XE-2100 if the Q-flags were adjusted. Q-Flags are adjustable settings that allow for the customization of the XE-2100 flagging sensitivities to meet the individual requirements of your laboratory. In reviewing the nucleated red blood cells (NRBC) enumeration capabilities we found the XE-2100 to have fewer FN than the CD-4000 for detection of NRBC's. The CD-4000 correctly enumerated NRBC's on 90% of the samples with NRBC's present. The XE-2100 correctly enumerated NRBC's on 97% of the samples with NRBC's. Stability studies were performed on both analyzers. The XE-2100 proved to be stable up to 48 hours for the WBC, RBC, HGB, HCT, MCV, PLT, NEUT%, LYMPH%, MONO%, EO% and BASO%. We also found most of the XE parameters stable well beyond 48 hours with the exception of the MONO% (48 hours at refrigerated temps) and MCV and MCHC, which were stable for 36 hours. The CD-4000 proved to be stable up to 36 hours for the WBC, RBC, HGB, HCT, MCV, PLT-I, PLT-O, NEUT%, LYMPH%, MONO%, EO% and BASO%. We found most of the CD-4000 parameters stable up to 48 hours with the exception of the EO%. The PLT-I and PLT-O comparisons of the XE-2100 and CD-4000 were good with r^2 values >0.90.

The XE-2100 is a fully automated hematology analyzer with simultaneous analysis of 32 parameters (26 reportable in the USA) including the NRBC and immature reticulocyte fraction (IRF) parameters. The XE-2100 uses several methodologies from previous Sysmex instrumentation along with a newly developed fluorescent optical detection unit for the following parameters: WBC, WBC differential, NRBC #, RET# and PLT-O #. The XE-2100 can process approximately 150 samples per hour, has various discrete analysis capabilities for cost-effective testing, and uses Windows NT system for easy operation.

(Sysmex J Int 11 : 22-26, 2001)

Key Words Automated Hematology Analyzer, XE-2100, Comparison, Q-Flags

INTRODUCTION

The Sysmex XE-2100 is a new automated hematology analyzer, which incorporates the analysis of nucleated red blood cells (NRBC) and reticulocytes (RET) including the immature reticulocyte fraction (IRF) parameter. The XE-2100 is fully automated and performs simultaneous analysis of 32 parameters (26 reportable in the USA). These parameters are: white blood cell (WBC), Neutrophil (NEUT) % and #, Lymphocyte (LYMPH) % and #, Monocyte (MONO) % and #, Eosinophil (EO) % and #, Basophil (BASO) % and #, NRBC % and #, red blood cell (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concntration (MCHC), RBC distribution width-coefficient of variation (RDW-CV), RBC distribution width-standard deviation (RDW-SD), RET%, IRF, high fluorescence ratio (HFR)*, middle fluorescence ratio (MFR)*, low fluorescence ratio (LFR)*, impedance platelet (PLT-I), optical platelet (PLT-O), mean platelet volume (MPV), PLT distribution width (PDW)*, PLT-large cell ratio (P-LCR)*, and plateletcrit (PCT)*. (*These parameters are not reportable in the USA.)

The XE-2100 can process approximately 150 samples per hour, has various discrete analysis capabilities for cost-effective testing, and uses Windows NT system for easy operation.

The XE-2100 performs hematology analyses using the following methods: RF/DC detection method, DC detec-

tion method with Hydrodynamic focusing, flow cytometry (FCM) using a semiconductor laser and non-cyanide SLS-hemoglobin method. The RF/DC detection method detects the volume of blood cells by changes in direct-current resistance, and the density of the blood cell interior by changes in radio-frequency resistance. Blood cells pass through the aperture of the detector surrounded by sheath fluid using the sheath flow method. The principle of FCM is similar to the SF-3000, although the entire optical unit is a new design. A semiconductor diode laser beam is emitted to the blood cells passing through the flow cell. The forward scattered light is received by a photodiode, and a photo multiplier tube receives the lateral scattered light and lateral fluorescent light. This light is converted into electrical pulses, thus making it possible to obtain blood cell information.

The XE-2100 employs FCM using a semiconductor diode laser to obtain information for the analysis for WBC 5-part differential, NRBC, RET, and optically measured fluorescent platelets (PLT). The semiconductor laser offers distinct advantages over the traditional Argon or Helium-Neon laser. These advantages include, rapid warm up to ready state, longer life cycle, lower power consumption, longer stability, and compact size. Using the RF/DC detection method as in previous Sysmex analyzer, the XE-2100 measure immature cell information in the IMI channel (immature myeloid information). The IMI channel serves to obtain information on the presence of immature granulocytes (IG), blasts, and hematopoietic progenitor cells (HPC).

HGB is measured with the non-cyanide SLS-hemoglobin method using Sodium Lauryl Sulfate, which is an analysis method used in previous Sysmex instrumentation.[1)]

The XE-2100 has four modes of sample introduction: manual mode (which requires approximately 130µL of sample), capillary mode (which requires approximately 40µL of blood for dilution), auto-sampler mode (which requires approximately 200µL of sample) and manual closed mode (which requires approximately 200µL of sample). The auto-sampler mode, which automatically mixes, aspirates, and analyzes samples without removing their caps, was used in this study.

The XE-2100 was compared to the Abbott Cell-Dyn 4000 (CD-4000) at Clarian Health Partners (CHP) for the following parameters: WBC, Neut%, Lymph%, Mono%, Eo%, Baso%, RBC, HGB, HCT, MCV, NRBC/100 WBC, PLT-I and PLT-O. Sensitivity studies were performed for both the overall flagging capabilities and for the NRBC enumeration capabilities. Stability studies were performed on both analyzers. PLT-I and PLT-O correlations were also performed.

MATERIALS AND METHODS

For this evaluation, residual material was used from patient specimens collected in K_3EDTA that was sent to the clinical laboratory at CHP for routine clinical testing. The XE-2100 analyzer was made available through Roche Diagnostic.

Roche Diagnostic's personnel calibrated the instrument upon installation according to the manufacturer's guidelines. Three levels of quality control material were used (Level 1, 2 and 3) throughout the duration of the study. The only maintenance performed on the XE-2100 performed was the daily shutdown, which entails approximately 1 minute of operator intervention. The majority of the shutdown process is fully automated.

The XE-2100 was compared to the Abbott CD-4000 hematology analyzer for the following parameters: WBC, NEUT%, LYMPH%, MONO%, EO%, BASO%, RBC, HGB, HCT, MCV, RET%, PLT-I, PLT-O and NRBC/100 WBC's. For this comparison, 251 whole blood specimens were analyzed, of which 1/3 fell within the laboratory's normal ranges. Specimens included samples with high WBC counts, high bilirubin, PLT clumps, NRBCs, IG, blast forms, left shift, atypical/abnormal LYMPH, iron deficiency, etc. Four hundred cell blind manual differentials were performed on all samples in this study (Two technologists performed 200 cell manual differentials each). The laboratory's positive criteria for the manual differential was > 10 bands, > 6 atypical LYMPH, >/=1 metas, myelos, pros, blasts or NRBCs. A stability study was performed on the XE-2100 using whole blood samples from three volunteer donors testing beyond 48 hours. CD-4000 was tested to only 48 hours due to servicing issues (CD-4000 manufacturer stated stability is 36 hours between 4 and 8 degrees C). After 8 hours the stability samples were stored at 4 degrees C.

RESULTS

As can be seen in ***Table 1A***, overall correlation between XE-2100 and CD-4000 for all measured parameters was excellent with r^2 values for most parameters > 0.90. Parameters with r^2 values <0.90 were MCV, MONO%, EO% and BASO%. The automated differentials were compared to the 400 cell manual differentials. The XE-2100 has the only fluorescent differential in the industry. The XE-2100 recovered slightly higher r^2 values than the CD-4000 when compared to the manual differential on the following parameters: NEUT%, LYMPH%, EO% and BASO% as shown in ***Table 1B.***

The correlation between the XE-2100 and the CD-4000 NRBC# and NRBC/100 WBC was very good. Correlation coefficients (r^2) were 0.98 and 0.96 respectively as shown in ***Table 2A.*** A total of 42 samples were positive for NRBCs on the 400 cell manual differential. The XE-2100 NRBC showed a higher correlation coefficient (r^2) than the CD-4000 when compared to the manual differential NRBCs. As shown in ***Table 2B***, the XE-2100 NRBC r^2=0.93 and the CD-4000 NRBC r^2=0.87. The XE-2100 had fewer false negatives (FN) on the NRBC enumeration than the CD-4000. As shown in ***Table 2C***, the CD-4000 had four FN NRBC samples. The NRBCs missed by the CD-4000 were 1.8 NRBC, 1.75 NRBC, 1.5 NRBC and 6 NRBCs (NRBCs are the average of 400 cell manual differentials). The XE-2100 had 1 FN NRBC sample. The XE-2100 reported 0.0 NRBC on one sample where 1.75 NRBCs were seen on the smear. The CD-4000 correctly enumerated NRBCs on 90% of the samples with NRBCs present. The XE-2100 correctly enumerated NRBCs on 97% of the samples with NRBCs. The XE-2100 utilizes a polymethine

Table 1A *Correlation results XE-2100 vs. CD-4000*

Parameter	n	r^2 value
WBC	246	1.00
NEUT%	221	0.96
LYMPH%	230	0.96
MONO%	232	0.82
EO%	240	0.80
BASO%	234	0.01
RBC	246	0.97
HGB	246	0.96
HCT	246	0.94
MCV	246	0.84
PLT-O	246	0.91
PLT-I	244	0.97

Table 1B *Manual diff correlations*

Parameter	XE-2100 vs. Manual Diff	CD-4000 vs. Manual Diff
NEUT%	r^2=0.94	r^2=0.93
LYMPH%	0.91	0.87
MONO%	0.73	0.75
EO%	0.90	0.7
BASO%	0.07	0.0

Table 2A *NRBC Correlation XE-2100 vs. CD-4000*

Parameter	r^2 value XE vs. CD
NRBC#	0.98
NRBC%	0.96

Table 2B *Automated NRBC vs. Manual Diff NRBC*

Instrument	NRBC Manual Diff
XE-2100 NRBC	r^2 =0.93
CD-4000 NRBC	r^2 =0.87

Table 2C *NRBC FN*

Instrument	#FN Samples with NRBCs	NRBCs missed on each sample
CD-4000	4	1.8 1.75 1.5 6
XE-2100	1	1.75

dye specific for nucleic acid for NRBC enumeration. The CD-4000 utilizes the propidium iodide dye for its NRBC enumeration.

The PLT-I on both instruments was compared. The r^2 value for the PLT-I was 0.97. The XE-2100 fluorescent PLT-O was compared to the CD-4000 PLT-O. The XE-2100 has the only fluorescent PLT-O on the market. The r^2 value for the PLT-O of the XE-2100 and CD-4000 was 0.91.

A limited stability study was performed on whole blood from three normal volunteers. The XE-2100 proved to be stable well over 48 hours for the WBC, RBC, HGB, HCT, MCV, PLT, NEUT%, LYMPH%, MONO%, EO% and BASO%. We also found most of the XE parameters stable greater than 48 hours with the exception of the MONO% (48 hours at refrigerated temps) and MCV and MCHC, which were stable for 36 hours. (The manufacturer stated stability is 48 hours for refrigerated samples on the above parameters except for MCV and MCHC, which are stable for 36 hours.) On the CD-4000 the WBC, HGB, HCT, MCV, PLT-I and PLT-O proved to be stable up to 48 hours. (CD-4000 manufacturer stated stability is 36 hours between 4 and 8 degrees C and for the above parameters). Samples could not be run beyond 48 hours due to servicing of the CD-4000.

The sensitivity study showed that the XE-2100 had a significantly lower FN rate than the CD-4000 (XE-2100 FN= 4, CD-4000 FN =14). The CD-4000 had fewer false positive (FP) than the XE-2100 (CD FP=13, XE FP = 37). The XE-2100 was set at a very sensitive level. The XE-2100 has a unique flagging feature called Q-flags. The Q-flag is a set of bar charts that are a visualization of the computer generated flagging for each sample. When the bar surpasses the 100% level the bar turns red and the flag is generated. Below the threshold the bar is green and no flag is generated. This threshold is adjustable which allows “customization” of the flagging. The Q-flag enables the laboratory to perform studies on each flag and determine at what level the threshold should be set to based on their patient population and the manual differentials performed by their medical technologists. During this study the Q-flag page was printed for every sample included in the sensitivity study to prove at what level each flag fell for each sample. The Q-flag printout allowed us to project what would happen if the thresholds were set differently based on the 400 cell manual differential. This Q-flag data is stored for each of 10,000 samples in the XE-2100 information-processing unit. For the original sensitivity study the Q-flag were left at default settings for all parameters. With optimization of the Q-flags at CHP, it could be projected that the XE-2100 could achieve both a lower FN and FP rate than the CD-4000. The XE showed a 35% lower FN rate than the CD-4000 with Q-flag adjustments while also achieving a 15.4% lower FP rate than that of the CD-4000 (XE with Q-flags adjustments- true positive (TP)=62, true negative (TN)=163, FN= 9, FP=11) as shown in ***Table 3A and 3B***.

Table 3A *Flagging sensitivity study*

	CD-4000	XE-2100	XE-2100 with Q-flag adjustments
TN	161	137	163
TP	57	67	62
FN	14	4	9
FP	13	37	11

Table 3B *Sensitivity study calculations*

	CD-4000	XE-2100	XE-2100 with Q-flag adjustments
Sensitivity	80.3%	94.4%	87.3%
Specificity	92.5	78.7	93.7
Predictive value % Positive	81.4	64.4	84.9
Predictive value % Negative	92	97.1	94.8
Efficiency	88.9	83.3	91.8

Table 4A *CD-4000 FN-Total= 14*

Sample No.	FN's on CD-4000
2	1 meta
3	1 myelo
8	13.5 bands
21	2 meta, hypersegmented neutrophils
29	30.5 bands
43	1.5 meta
74	1 meta
100	1.5 meta
120	clot, 14.5 bands
143	1 meta
163	2 meta, 1 myelo
166	1 meta
171	1 myelo
176	1 meta

Table 4B *XE-2100 FN-Total= 4*

Sample No.	FN's on XE-2100
2	1 meta
166	1 meta
171	1 myelo
176	1 meta

Table 4C *XE-2100 FN with Q-flag adjustments-Total= 9*

Sample No.	FN's XE-2100 with Q-flag adjustments
2	1 meta
166	1 meta
171	1 myelo
176	1 meta
3	1 myelo
43	1.5 meta
45	1 meta
62	1 meta
74	1 meta

The Q-flags allow customization of the flagging so that a suitable "balance" in flagging is achieved for each lab. It is the responsibility of each laboratory to appropriately validate and approve potential changes in performance. The FN for each analyzer are listed in ***Table 4A, 4B, and 4C***.

Note: Q-Flags are usually left at the defalt settings during evaluations, as the flagging sensitivity desired for each individual laboratory is not known. The projections of Q-flags made during evaluations are not used when instruments are installed since this is on a limited number of patient samples. A study to determine the appropriate Q-Flag setting for each laboratory can be performed once the analyzer is installed.

DISCUSSION AND CONCLUSION

Correlation between the XE-2100 and the CD-4000 showed good results for all complete blood count (CBC) and the WBC differential parameters. The XE-2100 is able to provide accurate and reliable results over a wide range of abnormal sample types.

The XE-2100 utilizes a newly developed fluorescent optical detection method for PLT in conjunction with the proven hydrodynamically focused impedance method, which enhances the reliability of PLT counting. The XE-2100 employs a FCM using a semiconductor laser similar to the SF-3000 to obtain information for the analysis of WBC 5-part differential, NRBC, RET, and fluorescent PLT-O. The semiconductor laser offers distinct advan-

tages over traditional lasers. These advantages include: longer life cycle, much shorter warm up time to ready state, lower power consumption, longer stability, and smaller size. HGB is measured with the non-cyanide SLS-hemoglobin method using Sodium Lauryl Sulfate, which is an analysis method used in previous Sysmex instrumentation. Utilizing the RF/DC detection method as in previous Sysmex instruments, the XE-2100 measures immature cell information in the IMI channel, which provides information on the presence of IG, blasts, and HPC. In addition, the XE-2100 is easy to operate and requires little maintenance. Maintenance for the study period was as simple as executing a bleach shutdown each day. No other maintenance was necessary or performed.

In conclusion, the Sysmex XE-2100, automated hematology analyzer, performed very well compared to the CD-4000. The XE-2100 provides accurate and reliable NRBC enumeration capabilities. The XE-2100 NRBC enumeration proved to be more sensitive than the CD-4000 NRBC enumeration, having a lower FN rate than the CD-4000. The XE-2100 at baseline Q-flag settings had a significantly lower FN rate. The FP were higher on the XE-2100 compared to the CD-4000. However, with Q-flag adjustments the XE-2100 could achieve a lower FN and FP rate compared to the CD-4000. The use of the XE-2100 should enhance the quality of result reporting and add efficiency by optimizing human resources in the hematology laboratory.

References

1) *Pearson RW, Houwen B, and Mast B: SULFOLYSER automated hemoglobin reagent-Introduction of a new cyanide-free method. Monograph, TOA Medical Electronics (USA), Inc. 1991.*
2) *Gould N, et al.: Performance evaluation of the sysmex XE-2100, automated hematology analyzer. Sysmex J Int, 9: 120-128, 1999.*
3) *Inoue H: Overview of automated hematology analyzer XE-2100. Sysmex J Int, 9: 58-64, 1999.*
4) *International Committee for Standardization in Hematology (ICSH): Protocol for evaluation of automated hematology analyzer. ICSH, 6: 69, 1984.*
5) *Machin SJ, et al.: Improved platelet counting on a new automated blood cell counter. Poster Abstract Laboratory Hematology, 5: 99, 1999.*
6) *Weber N, Mast BJ, and Houwen B: Performance evaluation of hematology analyzers: An outline for clinical laboratory testing. Sysmex J Int, 5: 103-113, 1995.*
7) *Zini G, et al.: Automated counting of nucleated red blood cells (NRBC): Evaluation of the sysmex XE-2100 system. Poster Abstract Laboratory Hematology, 5: 94, 1999.*