Hematology Focus
Ultra-Low Linearity
May 2006

POINTS TO CONSIDER WHEN ASSESSING THE LOW END OF LINEAR RANGE IN CELL COUNTS

Lisa Jarvis, Ph.D., MT (ASCP)

Testing the capabilities of hematology instruments for cell counting at very low numbers of cells has become more and more important in the clinical laboratory. One of the most frequent needs to analyze low cell counts is also one of the most critical: the low platelet count in the case of chemotherapy or platelet transfusions to patients receiving chemotherapy, platelet concentrations at which a decision to transfuse will be made have been decreased to very low values [1,2].

Other reasons for interest in testing the capabilities of hematology instruments for cell counting at very low numbers of cells are related to the increasing automation of body fluid counts. General hematology instruments are being validated for counting cerebrospinal fluid or other body fluids (Beckman Coulter LH750[3], Abbott CD3200[4] and others) or software methods appropriate for these fluids are being added to instruments (Advia 120 CSF[5], Sysmex XE2100 XE-Pro). Cell numbers in these fluids are usually much lower than those seen in peripheral blood and even relatively low numbers of cells can be clinically significant.

R&D Systems, is proud to offer our CBC-LINE products to assist the laboratory in monitoring the linear response of their hematology analyzers. This family of products is manufactured using gravimetric dilutions of cell concentrates with a plasma-like diluent. When combined with accurate calibration of the instrument, this approach gives the best available data to determine the reportable range of your hematology instrument. We have recognized a need for an Ultra-Low set that encompasses very low WBC and PLT counts within this family of products. When the capabilities of the instrument are being challenged by analysis of samples with very low cell numbers, it is critical to interpret CBC-LINE results carefully and be fully aware of factors contributing to accuracy that cannot be tested by any kit. Platelet counting will be used as the example throughout this document, although the statements are applicable to other parameters measured on the CBC-LINE kit.

Reportable range and clinical reportable range

Your CBC-LINE data allows a reportable range to be given in the analysis document. Clinical reportable range may be somewhat different from this range. At counts above the high end of the range, samples can be diluted in order to allow clinical reportable range to extend to higher values than analytical reportable range. At counts toward the low end of the range, it will be necessary to determine the acceptable level of precision, to screen for artifacts or confirm results with an alternate method and the clinical significance of the results when determining the clinical reportable range.

Matrix Effects

Low numbers of cells are often counted in the presence of relatively high numbers of other cell types in an abnormal patient sample. This is not reproduced by the gravimetric dilutions in CBC-LINE. Since CBC-LINE samples consist of stabilized cells in an artificial plasma-like medium, the analyzer may not always analyze the cells exactly as it would a patient sample. However, CBC-LINE makes it possible to challenge your instrument at cell counts that rarely occur in patient samples, and when they do occur are often accompanied by their own matrix effects that

Continued on page 2

may be detrimental to obtaining accurate counts. The results you get with the Ultra-Low linearity set should therefore be considered a test under optimum conditions reflecting the best results that could be obtained from abnormal patients.

Artifacts or clinical conditions that influence cell counts

Patient samples with low cell counts, especially low platelets counts, are prone to artifacts that affect accurate recovery (6). Aggregation of cells due to activation of cell surface adhesion molecules or clotting factors would interfere with linear response of cell counting. Cell fragments that count as platelets by some methods may be present; an example of this would be WBC fragments that may occur in myeloma (7). Thrombocytopenic patients in the recovery phase who have normal or near-normal hematopoiesis may have a high proportion of young, large platelets that may challenge threshold determinations during platelet counting which may in turn cause a falsely low platelet count. Clumps of two to three platelets can cause a falsely decreased platelet count (and high apparent MPV), possibly without triggering flags on some instruments (8). Although most instruments have "giant platelet" or "platelet clump" flagging capabilities, the software generating these flags is not 100% accurate. Presence of red cell fragments or other debris of similar size to that of platelets can cause artificially high platelet counts. Debris in the reagent or sample could be falsely counted as platelets. Even yeast, bacteria or malarial parasites have been reported to count as platelets on rare occasions. All these situations that affect the accuracy of platelet counting can be detected on a properly prepared and stained smear (6,10). The same smear or an alternate method can allow confirmation of the low platelet count (6,10,11). Since artifacts that could be present in a patient sample would not present at the time CBC-LINE samples are run, patient samples must be screened for them even when the results are within the reportable range determined from your CBC-LINE results.

How should I use the Ultra-Low CBC-LINE data to set reportable range limits?

Reports from CBC-LINE include a reportable range based on your results and the allowable +/- error you have specified. An instrument manufacturer's stated error limits could be used as a guideline. However, if the allowable clinical error of an expected experimental value designed for a particular kit level can be interpreted more broadly, then the manufacturer's limits may be overly tight. Narrow instrument performance limits can be attributed to statistical descriptions of analytical performance models used by manufacturers and should always be examined for clinical appropriateness. Alternatively, the manufacturer's performance limits may not be tight enough in the case of a low expected experimental value produced for the ultra low range evaluation where the allowable clinical error is much less. Again, the allowable clinical error of a platelet count of 10×10^3 / mL would be especially narrow at an institution where this value is the cutoff for prophylactic platelet transfusion. A manufacturer's stated linearity down to zero platelets with an uncertainty of +/- 10×10^3 / mL would not be adequate due to the reduced allowable clinical error of very low platelet counts. The acceptable performance limits for ultra low platelet and WBC values that are to be tested will depend on the allowable clinical error determined by the laboratory for each level tested and the analytical requirements for their patient population. The judgment of the Laboratory Director or Pathologist should also depend on a number of other factors not related to the results of your instrument on the CBC-LINE kit, such as your laboratory's criteria for confirmatory testing and delta checks.

What do my Ultra-Low CBC-LINE results tell me about accuracy of very low cell numbers?

Accuracy is determined by accurate calibration of the instrument, which must be performed independently. Hematology instruments are calibrated using a single point calibration, so combining accurate calibration with linearity determinations using CBC-LINE products having a reference value close to the calibration point should allow you to determine the accuracy of your instrument at other points. All instruments display a higher percentage difference from expected values at very low counts. Comparison of instrument values from patient samples with

very low platelet values to the flow cytometry reference method or to manual counting has shown that most hematology instruments have at least some bias on patient samples, generally over-estimating them somewhat (8,9).

What do my Ultra-Low CBC-LINE results tell me about precision of very low cell numbers?

At least four replicates are recommended per level. If smaller quantifiable mean differences between test concentrations are desired, larger numbers of replicates may be necessary and can be statistically determined. For a statistically significant determination of precision, reproducibility of the four replicates will give a reasonable estimate of precision.

What do regulatory agencies recommend regarding reporting of low cell numbers?

The International Society for Laboratory Hematology (ISLH) International Consensus Group for Hematology Review has published a guideline of criteria for review of patient results in Hematology (http://www.islh.org/2004/Committees ConsensusGroup /CGICGHReview.htm**)**. The guideline calls for using a second method to verify platelet counts and absence of artifacts when the platelet count is less than 100×10^3 / mL and the patient has no prior low count, if there is a delta check (as defined by the lab) or if an instrument flag is present. CLSI document EP6-A addresses linearity but does not specifically address how to find the lower limit that may be reported without confirmation. Accrediting agencies such as CLIA, JCAHO and CAP require determination of reportable range at the time a new instrument is evaluated. At the present time, ongoing testing at very low counts cannot be required due to the lack of QC materials that challenge these limits.

What are LoB, LoD and LoQ? Does the Ultra-Low CBC-LINE kit measure them?

CLSI (former NCCLS) approved guideline EP17-A defines LoB is the limit of the blank, or the highest result that indicates no amount of analyte (in this case, cells) are present. LoD is the limit of detection or the lowest amount of analyte that can be discriminated from zero with a stated probability, for example 95%. LoQ is the lower limit of quantitation. It is the lowest amount of analyte that can be reliably detected (above the LoD) and at which the total error meets the laboratory's requirements for accuracy. LoQ is therefore always greater than LoD, and the difference will be greatest when the requirement for accuracy is greatest. These values would be difficult for an individual clinical hematology laboratory to determine as recommended in the EP17-A document. A minimum of 60 measurements of one or several patient samples without the analyte (cells) are recommended for determining the 95% confidence value for LoB, and a pooled SD from 60 measurements from 4-6 patient samples with low values are recommended to calculate the LoD.

The CBC-LINE Ultra-Low kit does not include a blank for measuring the LoB. If low levels from the kit were used for measurements to determine the LoD, it would be with the understanding that these do not fully mimic patient samples, especially since RBC are not present and WBC and platelets are stabilized, normal cells.

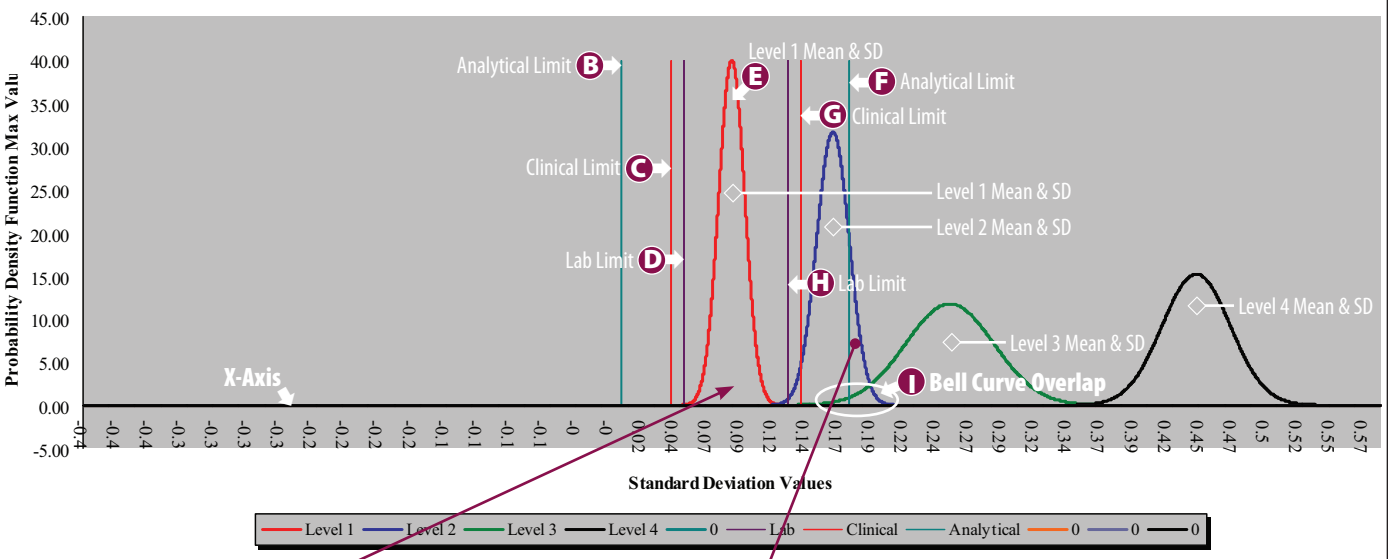
Advantages of the Ultra-Low CBC-LINE kit

Use of the Ultra-Low CBC-LINE kit will help the user determine the lower limit of linear response and give an estimate of precision and accuracy of their hematology instrument at very low WBC or platelet counts. Combined with confirmatory tests to rule out the presence of artifacts in the patient sample, the results obtained from the Ultra-Low CBC-LINE kit should allow the Laboratory Director or Pathologist to determine the lowest patient values that can be reported with confidence.

Continued on page 8

Example: Measurement Error Probability Analysis

Probability Distributions for Mean & SD



Analyte	Lab	R&D Systems / Verified Medical Research	Address	614 McKinley Place, N. E.				
WBC	City	Minneapolis	State	MN	Zip	55413	Date	3/4/2006

CBC-LINE Ultra Low Range Kit

Performance Limits

A Reference Target	Limit Type	+/- Value			Inst.
0.088	Lab	0.04		0	sn/ID
	Clinical	0.05		0	
	Analytical	0.088		0	

Probability of Exceeding Performance Limits

Inst./Meth.	Curve Data		% Mean Diff.	@ - Limit	@ + Limit	@ - Limit	@ + Limit	@ - Limit	@ + Limit	Total for	Total for	Total for
Name	Mean	SD	From Target	Analytical	Analytical	Clinical	Clinical	Lab	Lab	Analytical	Clinical	Lab
Level 1	0.085	0.01	-3.41%	0.00%	0.00%	0.00%	0.00%	0.01%	0.00%	0.00%	0.00%	0.01%
Level 2	0.163	0.0126	85.23%	0.00%	15.15%	0.00%	97.67%	0.00%	99.73%	15.15%	97.67%	99.73%
Level 3	0.253	0.034	187.50%	0.00%	98.84%	0.00%	99.97%	0.00%	99.99%	98.84%	99.97%	99.99%
Level 4	0.443	0.0263	403.41%	0.00%	100.00%	0.00%	100.00%	0.00%	100.00%	100.00%	100.00%	100.00%

Probability estimates for Level 1 mean recovery and differentiating the Level 2 and Level 3 test kit vial ratio cell concentrations from the quantified least amount detectable, LOD, target value at three laboratory defined allowable total error limits are:

			Lab	%Prob. of within	Clinical	%Prob. of within	Analytical	%Prob. of within
Level 1 Mean	Level 1 SD	Target	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery
0.085	0.01	0.088	0.04	99.99%	0.05	100.00%	0.088	100.00%

			Lab	% Prob. of Diff.	Clinical	% Prob. of Diff.	Analytical	% Prob. of Diff.
Level 2 Mean	Level 2 SD	Target	+/- Total error	from Target	+/- Total error	from Target	+/- Total error	from Target
0.163	0.0126	0.088	0.04	99.73%	0.05	97.67%	0.088	15.15%

			Lab	% Prob. of Diff.	Clinical	% Prob. of Diff.	Analytical	% Prob. of Diff.
Level 3 Mean	Level 3 SD	Target	+/- Total error	from Target	+/- Total error	from Target	+/- Total error	from Target
0.253	0.034	0.088	0.04	99.99%	0.05	99.97%	0.088	98.84%

Quantified Ultra Low Cell Concentration Performance Summary

	Ratio Target	Test Mean	Abs. Mean Diff.	Mean % Diff.	SD	%CV
Level 1	0.088	0.085	-0.003	-3.41%	0.01	11.76%
Level 2	0.176	0.163	-0.013	-7.39%	0.0126	7.73%
Level 3	0.264	0.253	-0.011	-4.17%	0.034	13.44%
Level 4	0.44	0.443	0.003	0.68%	0.0263	5.94%
Level 5	0.879	0.885	0.006	0.68%	0.0332	3.75%
Level 6 (Ref.)	8.79	8.79	0	0.00%	0.0347	0.39%

What to look for:

1. **Quantifiable Concentration Detection**
   - **a.** Minimum +/– bias from ratio target.
   - **b.** Minimum replicate SD (not 0 SD).
   - **c.** Minimum bell curve overlap, clear bell curve separations on the x-axis.
2. **Reasonable Total Error Limits**
   - **a.** Manageable +/– allowable error limits for observed bias and SD.
   - **b.** Acceptable % probability of within limit recovery for LOD mean & SD.
   - **c.** Maximum % probability of differentiating higher concentrations from LOD +/– total error limits.
   - **d.** LOD total error limits that are so wide that they would not permit a significant % probability of higher concentration differentiation.
   - **e.** LOD total error limits that are so narrow that they are not practical to manage nor detectable by the instrument's reporting decimal fraction.

Minimum Measurement Error at Each Concentration Tested

Definitions for Measurement Error Probability Analysis

A Reference Target

Limit Qualified Lowest Amount Detected LOD. The target value is qualified as acceptable when the observed mean recovery is within the +/- limits of the allowable total error for the target value.

B Analytical Limit

This vertical mark represents the largest negative allowable error limit boundary chosen for the Reference TARGET value. Typically, this value is the absolute difference between the Reference TARGET and the next largest ratio target value concentration. Any portion of a bell curve that extends to the left of this line represents the % probability for negative ANALYTICAL limit failure of a single result.

C Clinical Limit

This vertical mark represents the negative allowable CLINICAL total error limit boundary chosen for the test recovery mean and SD of the Reference TARGET ratio concentration vial. Typically, this value is chosen or accepted by the laboratory to represent the absolute allowable total error CLINICAL difference between the Reference TARGET ratio concentration value and the observed mean and associated SD of the Reference TARGET vial replicate results. Any portion of a bell curve that extends to the left of this line represents the % probability for negative CLINICAL limit failure of a single result.

D Lab Limit

This vertical mark represents the negative allowable LAB total error limit boundary chosen for the test recovery mean and SD of the Reference TARGET ratio concentration vial. Typically, this value is chosen or accepted by the laboratory to represent the LAB absolute allowable total error difference between the Reference TARGET ratio concentration value and the observed mean and associated SD of the Reference TARGET vial replicate results. Any portion of a bell curve that extends to the left of this line represents the % probability for negative LAB limit failure of a single result.

E Level 1 Mean & SD

This is the probability distribution for measurement error associated with the Level 1 replicate analysis. The total area under the bell curve represents 99.999% of the possible measurement error that could be expected for a single result at this concentration. The peak of the bell curve represents the mean of Level 1 replicate data. The mean value of the replicate data will define the amount of left or right position (BIAS) from the target value marked on the X-axis. The spread of the bell curve is determined by the standard deviation, SD, which is calculated from the mean and the individual test replicate differences. The larger the SD, the greater is the spread of the bell curve. The greater the bias, +/- difference between the target and observed mean, the greater the +/- distance from the target value marked on the X axis. The bias and SD describe the position and spread of the entire bell curve along the X-axis. The bell curve describes the probability for measurement error found at this concentration in equal and opposite directions from the mean. The analytical goal is to evaluate how well the mean agrees with the target and how well one target concentration can be quantitatively differentiated from the next target concentration.

F Analytical Limit

This vertical mark represents the largest positive allowable error limit boundary chosen for the Reference TARGET value. Typically, this value is the absolute difference between the Reference TARGET and the next largest ratio target value concentration. Any portion of a bell curve that extends to the right of this line represents the % probability for positive ANALYTICAL limit failure of a single result.

G Clinical Limit

This vertical mark represents the positive allowable CLINICAL total error limit boundary chosen for the test recovery mean and SD of the Reference TARGET ratio concentration vial. Typically, this value is chosen or accepted by the laboratory to represent the absolute allowable total error CLINICAL difference between the Reference TARGET ratio concentration value and the observed mean and associated SD of the Reference TARGET vial replicate results. Any portion of a bell curve that extends to the right of this line represents the % probability for positive CLINICAL limit failure of a single result.

H Lab Limit

This vertical mark represents the positive allowable LAB total error limit boundary chosen for the test recovery mean and SD of the Reference TARGET ratio concentration vial. Typically, this value is chosen or accepted by the laboratory to represent the LAB absolute allowable total error difference between the Reference TARGET ratio concentration value and the observed mean and associated SD of the Reference TARGET vial replicate results. Any portion of a bell curve that extends to the right of this line represents the % probability for positive LAB limit failure of a single result.

I Bell Curve Overlap

This bell curve overlap represents the relative % probability for single result values to occur within the measurement error of either concentration's observed mean and SD. In this example, Levels 2 and 3 bell curves overlap producing a % probability for reporting a Level 3 value as a Level 2 concentration and a second % probability for reporting a Level 2 value as a Level 3 concentration. Usually, a visual inspection is sufficient to determine the allowable degrees of bell curve overlap, however, additional plot analysis can determine the exact % probability for either degree of bell curve overlap. Please contact Verified Medical Research at 480-732-0808, or vmresearch@worldnet.att.net to request information regarding fees for additional analysis services.

The Effects of Decimal Fraction Rounding Conventions on Measurement Error Analysis

The quality of measurement error quantification will be greatly affected by the reportable decimal fraction rounding convention being employed for test results. As the requirement for measurement information expands, so should the decimal fraction of the reported test results. Measurement error quantification is greatly inflated by using a reporting decimal fraction that is too large. If there is too large of a reporting decimal fraction associated with very low concentrations, critical measurement information could be lost. If possible, and if the measurement method can credibly detect the desired diagnostic decimal fraction, it is wise to reveal and analyze the most expanded decimal fraction available for the test results.

I would like to provide you with two examples of test result decimal fraction rounding and its effect on the quality of meas urement error analysis. The first example will examine a possible set of test results for a .08 WBC cell concentration challenge. The following table (Table 1) will list four replicate test result examples with three decimal fraction rounding conventions.

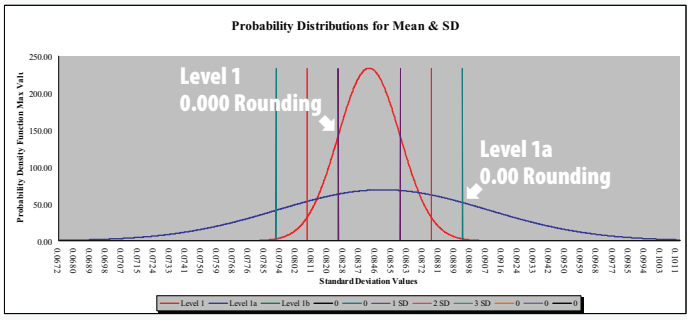
A plot of the measurement error probabilities based on the means and SD's will reveal the impact on the quality of measurement error quantification. The probability for increased error probability can be calculated in table 2 below.

Using the mean, (.08425), and SD, (.001708), estimates from the Level 1 replicate results, that use a .000 reporting decimal fraction convention as a target performance reference, there is a 45.27% increase in allowable measurement error probability for the Level 1a, (.00 decimal fraction convention), mean, (.085), and SD, (.005744), estimates at the +/- 1 SD limit, a 51% increase at the +/- 2 SD limit, and a 37.78% increase at the +/- 3 SD limit.

Table 1: Rounding Conventions

Replicate	(1) 0.000	(1a) 0.00	(1b) 0.0
1	0.082	0.08	0.1
2	0.085	0.09	0.1
3	0.086	0.09	0.1
4	0.084	0.08	0.1
Mean	0.08425	0.085	0.1
SD	0.001708	0.005774	0
%CV	2.03	6.79	0

By reducing the decimal fraction rounding convention to .0 for the Level 1b replicate data, there is a total loss of replicate measurement error information, no SD, and therefore, there can be no plot of the measurement error probability for Level 1b replicate data. The reduction in the decimal fraction convention to .0 also inflates the error in the mean estimate of the replicate data. In this example, the rounding convention of .0 causes a difference of 18.69% between the Level 1 mean, (.08425), and the Level 1b mean, (.1).



Depending on the laboratory's diagnostic requirements for ultra low WBC cell counts, the laboratory will need to investigate their instrument's reporting decimal fraction conventions and method capabilities. It should not be assumed that ultra low WBC cell counts could be quantified employing a reporting decimal fraction that is larger than that which is anticipated to be diagnostic for the laboratory's application.

Table 2:

			1 SD	%Prob. of within	2 SD	%Prob. of within	3 SD	%Prob. of within
Level 1 Mean	Level 1 SD	Target	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery
0.08425	0.001708	0.08425	0.001708	68.27%	0.003416	95.45%	0.005124	99.73%

			1 SD	%Prob. of within	2 SD	%Prob. of within	3 SD	%Prob. of within
Level 1a Mean	Level 1a SD	Target	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery
0.085	0.005774	0.08425	0.001708	23.00%	0.003416	44.45%	0.005124	61.95%

			1 SD	%Prob. of within	2 SD	%Prob. of within	3 SD	%Prob. of within
Level 1b Mean	Level 1b SD	Target	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery
0.1	0	0.08425	0.001708		0.003416		0.005124	

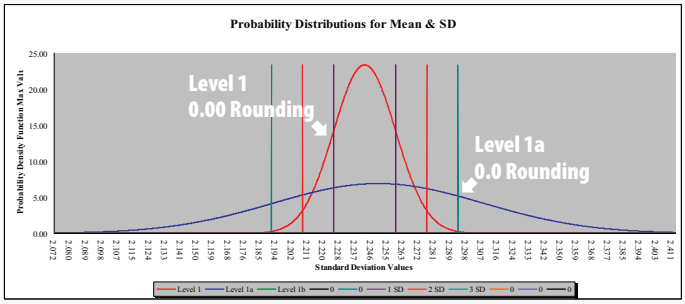
The second example of reporting decimal fraction convention effects on measurement error quantification will be test results for a 2.2 PLT cell concentration challenge. In order to retain the same error effect probability frame of reference, the same replicate error result-ending digits will be used for the Level 1 data. As in the prior example, the following table (Table 3) will list the four replicate test result examples with three decimal fraction-rounding conventions.

Table 3: Rounding Conventions

Replicate	(1) 0.00	(1a) 0.0	(1b) 0
1	2.22	2.2	2
2	2.25	2.3	2
3	2.26	2.3	2
4	2.24	2.2	2
Mean	2.2425	2.25	2
SD	0.017078	0.057735	0
%CV	0.76	2.57	0

A plot of the measurement error probabilities based on the means and SD's will reveal the impact on the quality of measurement error quantification. The probability for increased error probability can be calculated in table 4, below.

Using the mean, (2.2425), and SD, (.017078), estimates from the Level 1 replicate results, that use a .00 reporting decimal fraction convention as a target performance reference, there is a 45.27% increase in allowable measurement error probability for the Level 1a, (.0 decimal fraction convention), mean, (2.25), and SD, (.05744), estimates at the +/- 1 SD limit, a 51% increase at the +/- 2 SD limit, and a 37.78% increase at the +/- 3 SD limit. The



consistencies in measurement error inflation estimates for the PLT example are caused by the use of the same result-ending digits for the PLT replicate data as those used in the WBC example. The decimal fraction expansion was also controlled in the same way as those in the WBC example by powers of ten increments.

By reducing the decimal fraction rounding convention to 0 for the Level 1b replicate data, there is a total loss of replicate measurement error information, no SD, and therefore, there can be no plot of the measurement error probability for Level 1b replicate data. The reduction in the decimal fraction convention to 0 also inflates the error in the mean estimate of the replicate data. In this example, the rounding convention of 0 causes a difference of -10.81% between the Level 1 mean, (2.2425), and the Level 1b mean, (2).

Depending on the laboratory's diagnostic requirements for ultra low PLT cell counts, the laboratory will need to investigate their instrument's reporting decimal fraction conventions and method capabilities. It should not be assumed that ultra low PLT cell counts could be quantified employing a reporting decimal fraction that is larger than that which is anticipated to be diagnostic for the laboratory's application.

Table 4:

			1 SD	%Prob. of within	2 SD	%Prob. of within	3 SD	%Prob. of within
Level 1 Mean	Level 1 SD	Target	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery
2.2425	0.017078	2.2425	0.017078	68.27%	0.034156	95.45%	0.051234	99.73%
			1 SD	%Prob. of within	2 SD	%Prob. of within	3 SD	%Prob. of within
Level 1a Mean	Level 1a SD	Target	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery
2.25	0.057735	2.2425	0.017078	23.00%	0.034156	44.45%	0.051234	61.95%
			1 SD	%Prob. of within	2 SD	%Prob. of within	3 SD	%Prob. of within
Level 1b Mean	Level 1b SD	Target	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery	+/- Total error	Limit Recovery
2	0	2.2425	0.017078		0.034156		0.051234	

REFERENCES:

1. Norris S., Pantelidou D., Smith D., Murphy M. F. *Immunoplatelet counting: potential for reducing the use of platelet transufsions through more accurate platelet counting.* Br J Haematol. 2003; **121**:605-613.

2. Heddle N. M., Cook R. J., Webert K. E., Sigouin C., Rebulla. *Methodologic issues in the use of bleeding as an outcome in transfusion medicine studies.* Transfusion 2003; **43**:742-752.

3. Brown W., Keeney M., Chin-Yee I., Johnson K., Lantis K., Finn W., Wolfe N., Kaplan S. *Validation of Body Fluid Analysis on the Coulter LH 750.* Lab Hematology 2003; **9**:155-159.

4. Andrews J., Setran E., McDonnel L., Kussick S., Wood B. L., Sabath D. E. *An Evaluation of the Cell-Dyn 3200 for Counting Cells in Cerebrospinal and Other Body Fluids.* Lab Hematology 2005; **11**:98-106.

5. Aune MW *et al. Automated Flow Cytometric Analysis of Blood Cells in Cerebrospinal Fluid.* Hematopathology 2004; **121**:690-700.

6. Moreno A, Menke D. *Assessment of Platelet Numbers and Morphology in the Peripheral Blood Smear.* Clin Lab Med 2002; **22**:193-213.

7. Kunz D., Kunz W. S., Scott C. S., Gressner A. M. *Automated CD61 immunoplatelet analysis of thrombocytopenic samples.* Br J Haematol. 2001; **112**:584-592

8. Steele BW, Wu N-C, Whitcomb C. *White Blood Cell and Platelet Counting Performance by Hematology Analyzers: A Critical Evaluation.* Laboratory Hematology 2001; **7**:255-266.

9. Sandhaus L. M., Ebenezer S. O., Agrawal N. N., Dillman C. A., Meyerson H. J. *Platelet Counting by the Coulter LH 750, Sysmex XE 2100 and Advia 120.* Am J Clin Pathol 2002; **118**:235-241.

10. Sutor A. H., Grohman A., Kaufmehl K., Wundisch T. *Problems with Platelet Counting in Thrombocytopenia.* Sem Thromb Hemostasis 2001; **27**:237-243.

11. Harrison P. et al for the International Society of Laboratory Hematology Task Force for the Reference Platelet Count. *An Interlaboratory Study of a Candidate Reference Method for Platelet Counting.* Am J Clin Pathol 2001; **115**:448-459.

Quality | Selection | Performance | Results

R&D Systems
Hematology Division
614 McKinley Place NE
Minneapolis, MN 55413

phone 612-379-2956
toll free 800-428-4246
fax 612-656-4400
email HemeSales@RnDSystems.com

www.RnDHeme.com
www.RnDSystems.com