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White Paper

Performance Evaluation of LOCI Vitamin B12 and Folate Assays on the Dimension EXL integrated chemistry system with LOCI module

C. Briggs, T. Johnson, S. A. Lewisch, L. Schiavoni, J. Thomas, C. Tyler.

Answers for life.

Performance evaluation of LOCI Vitamin B12 and Folate assays on the Dimension EXL integrated chemistry system with LOCI module

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Abstract

Introduction

The objective of this study was to evaluate the performance of the fully automated LOCI® vitamin B12 (LOCI VB12) and folate (LOCI FOLA) assays for the Siemens Dimension® EXL™ integrated chemistry system with LOCI® module. The newly developed vitamin B12 and folate assays are homogeneous, competitive immunoassays based on Luminescent Oxygen Channeling Immunoassay (LOCI) technology. LOCI reagents include two synthetic bead reagents, chemibead and sensibead, and a biotinylated analyte receptor. The sensibead is coated with streptavidin and contains a photosensitive dye. The chemibead is coated with an analyte analog and contains a chemiluminescent dye as the signal generation component. Before the immunological portion of the reaction is initiated, the patient sample is pretreated with sodium hydroxide and dithioerythritol to release analyte from endogenous binding proteins. The assays are calibrated with the five level multi-analyte LOCI anemia calibrator. LOCI Vitamin B12 assay time is 32 minutes and LOCI folate is 21 minutes. Sample volume is 12 µL and 10 µL for the B12 and folate assays, respectively.

Methods

Precision estimates were obtained per CLSI EP05-A2 protocol (two replicates twice a day for twenty days) using quality control materials and human serum pools. Linearity was assessed through dilution of high and low analyte samples outside of the measuring interval. Specimen equivalence testing was performed with matched sets of serum and plasma samples. Method comparisons with patient samples were conducted versus vitamin B12 (VB12) and folate (FOL) assays on the Dimension Vista® system (X-axis). Accuracy was evaluated by recovery of the World Health Organization (WHO) Vitamin B12 and Folate International Standard 03/178.

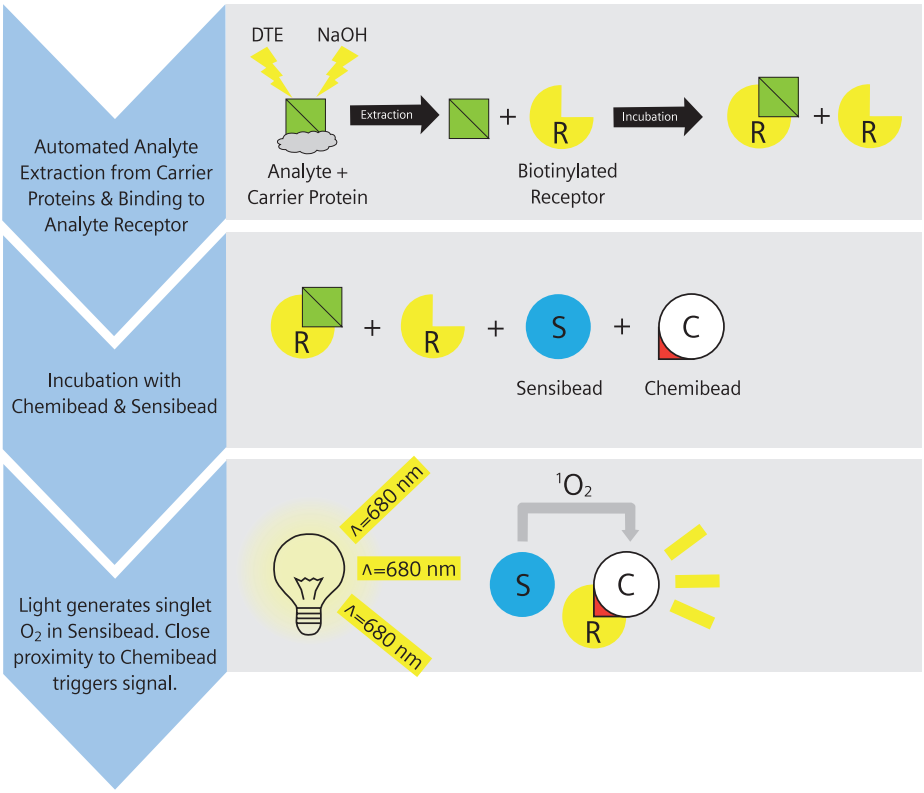
Results

Linearity was demonstrated throughout the measuring interval for the B12 assay of 80 to 2000 pg/mL and 0.5 to 20.0 ng/mL for the folate assay (intervals span from the LoQ for B12 and LoD for folate to the upper calibration standard). With automated dilution, the measuring interval is extended to 6000 pg/mL for B12 and 100 ng/mL for folate. Equivalent results were obtained among serum, and lithium and sodium heparin plasma for both B12 and folate assays and EDTA plasma for the B12 assay. B12 levels were tested at 180, 498, and 978 pg/mL and resulted in repeatability of 5.6%, 2.3% and 2.5%, and within-laboratory precision of 6.5%, 3.7% and 2.8%, respectively. Folate levels were tested at 2.1, 6.6, and 16.7 ng/mL and resulted in repeatability of 4.3%, 4.1% and 2.2%, and within-laboratory precision of 7.6%, 5.5% and 4.0%, respectively. Passing-Bablok regression statistics for Dimension EXL Vitamin B12 vs. Dimension Vista B12 were: slope: 1.00, intercept: -2.1, r: 0.999, n: 213, range: 62 to 1973 pg/mL. Simple linear regression statistics for Dimension EXL folate vs. Dimension Vista folate were: slope: 1.01, intercept: 0.05, r: 0.99, n: 138, range: 0.6 to 19.2 ng/mL. Recovery difference from the WHO Standard 03/178 was 2.1% (target 480 pg/mL) for B12 and -7.3% (target 5.33 ng/mL) for folate.

Conclusions

The study results demonstrate good performance of the fully automated vitamin B12 and folate assays on the Dimension EXL system.

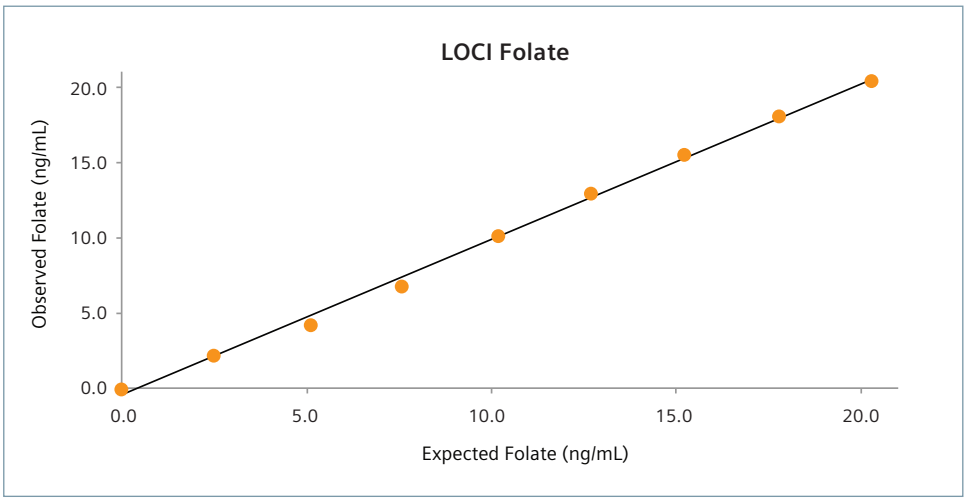
LOCI Technology & Reaction

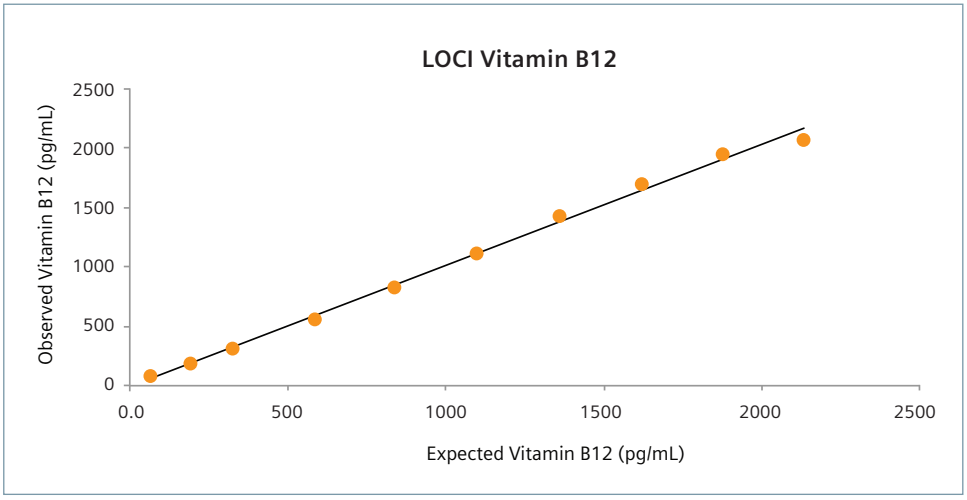


Assay Specifications

Attributes	LOCI Folate	LOCI Vitamin B12
Assay Time	21 minutes	32 minutes
Assay Range	0.5 to 20.0 ng/mL	80 to 2000 pg/mL
Sample Volume	10 µL	12 µL
Specimen Types	Serum, Plasma (Lithium Heparin and Sodium Heparin)	Serum, Plasma (Lithium Heparin, Sodium Heparin, and EDTA)
Calibrator	LOCI Anemia Calibrator	LOCI Anemia Calibrator

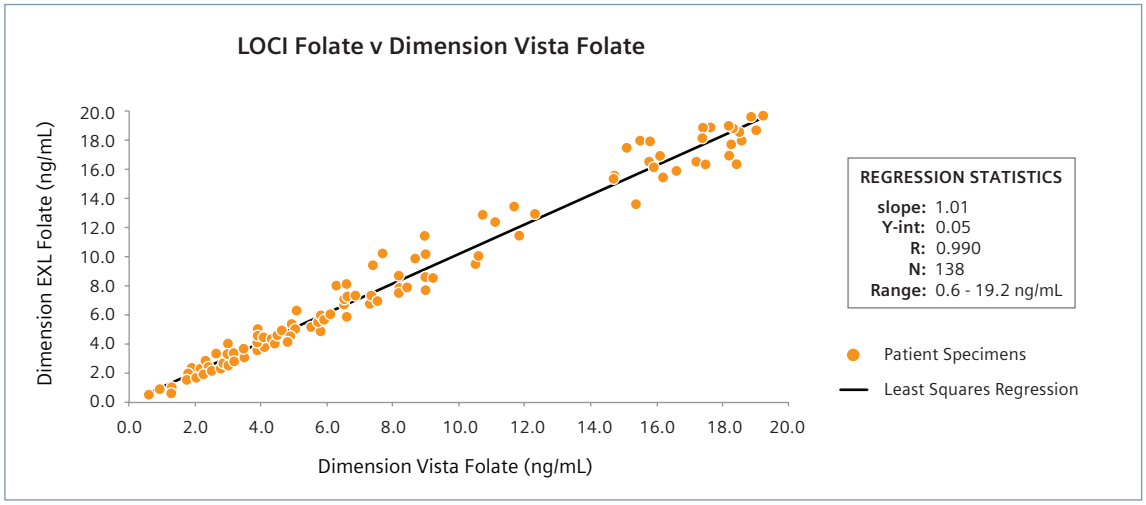
Assay Range Linearity



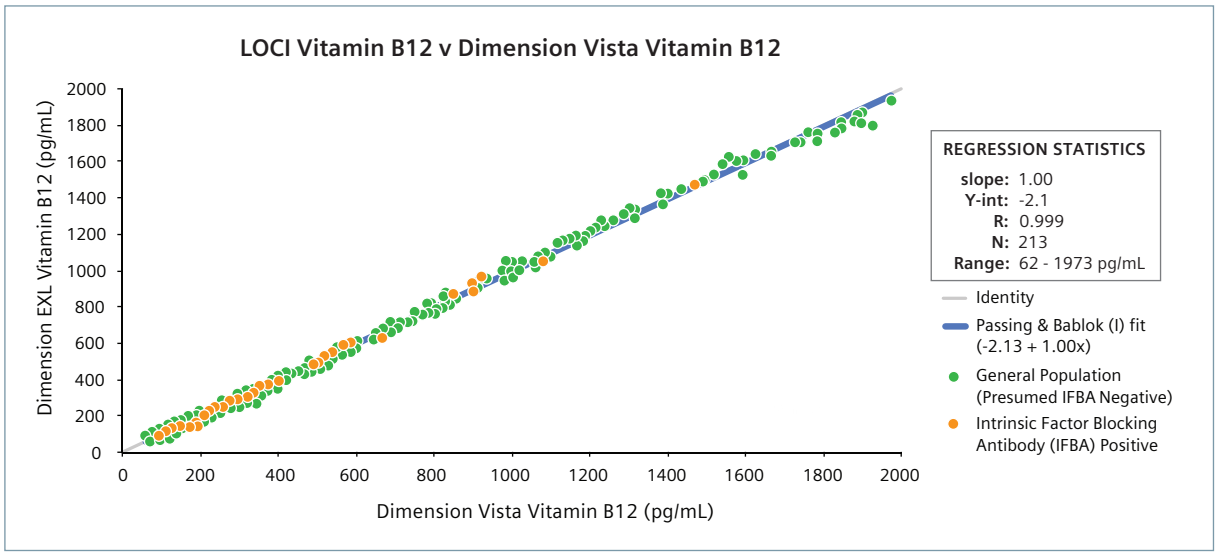


- Testing based on CLSI EP17-A2
- ≥ Nine levels of serum spanning the assay range
- Insignificant p-value for quadratic/cubic term or non-linearity of ≤ 10%

Method Comparison



- Testing based on CLSI EP9-A2
- Excellent correlation with Dimension Vista Folate
- Regression Type: Linear



- Testing based on CLSI EP9-A2
- Excellent correlation with Dimension Vista Vitamin B12
- Regression Type: Passing-Bablok
- Population: n=45 IFBA positive; n=168 General Population
- IFBA Samples consistent with general population

Precision

Assay	Sample	Average (ng/mL)	Precision (%CV)	
			Repeatability	Within-Lab
LOCI FOLA	QC Level 1*	2.1	4.3%	7.6%
	QC Level 2*	6.6	4.1%	5.5%
	Serum Pool	16.7	2.2%	4.0%
		(pg/mL)	Repeatability	Within-Lab
LOCI VB12	Serum Pool	180	5.6%	6.5%
	QC Level 2*	498	2.3%	3.7%
	Serum Pool	978	2.5%	2.8%

*QC Material: Biorad Liquichek™ Immunoassay Plus Control

- Testing based on CLSI EP5-A2
- Samples tested twice a day for 20 days
- Data calculated by Analysis of Variance (ANOVA)
- Low imprecision for both assays

Accuracy

(WHO International Standard for Vitamin B12 and Serum Folate 03/178)

Assay	Observed Recovery	Target Value	% Difference
LOCI FOLA	4.9 ng/mL	5.3 ng/mL	-7.3%
LOCI VB12	490 pg/mL	480 pg/mL	2.1%

- Excellent alignment with WHO Standard

Specimen

Assay	Comparative Specimen	Slope	Correlation Coefficient	n
LOCI FOLA	Lithium Heparin Plasma	1.01	0.995	25
	Sodium Heparin Plasma	0.99	0.979	25
LOCI VB12	Lithium Heparin Plasma	1.00	0.998	78
	Sodium Heparin Plasma	1.02	0.998	78
	EDTA Plasma	1.00	0.998	78

- Testing based on CLSI EP9-A2
- Comparison testing results versus a plain red top tube
- Excellent correlation between serum and plasma

Conclusions

LOCI Folate

- Fully automated assay on the Dimension EXL
- Repeatability ≤ 4.3%; Within-Lab Precision ≤ 7.6%
- WHO Bias of ≤ 7.3%
- High correlation between serum and plasma
- Excellent correlation with Dimension Vista predicate assay

LOCI VB12

- Fully automated assay on the Dimension EXL
- Repeatability ≤ 5.6%; Within-Lab Precision ≤ 6.5%
- WHO Bias of ≤ 2.1%
- High correlation between serum and plasma
- Excellent correlation with Dimension Vista predicate assay
- IFBA positive samples consistent with general population samples

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