MAGELLAN BIOSCIENCES

CLINICAL REVIEW

Review of the Performance Characteristics of the LeadCare® II Blood Lead Testing System

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INTRODUCTION

Blood lead concentrations have decreased in US children, but approximately 25% still live in housing with deteriorated lead-based paint and are at risk of lead exposure.[1] "*Most US children are at sufficient risk that they should have their blood lead concentration measured at least once*".[1] Despite federal mandates to screen young children enrolled in Medicaid, an estimated 80% have never been tested. [2,3] A Government Accounting Office (GAO) review of Medicaid screening rates for lead poisoning found that only 19% of 1-5 year old children received a blood lead test.[4,5] As a result, most children with elevated lead levels are not identified and go untreated.

Traditional laboratory methods for lead screening are expensive and complicated to use. Physicians usually refer a child to an outside laboratory for the test or draw the blood sample themselves and mail it to the lab. The physician waits, in some cases, weeks before receiving the results. During this delay patients frequently relocate making follow-up care difficult or impossible. Adding to the challenges of lead screening is that many parents do not take their children to the laboratory as the physician requested.[6] As a result; screening rates continue to suffer along with the young children who are exposed to lead and remain untreated.[7]

Responding to the need to improve lead screening rates, the CDC awarded ESA Biosciences Inc. a contract to develop a new portable blood lead testing system that would meet the CLIA requirements for waiver. The availability of a waived test is predicted to increase screening rates among children that need it most. In the past, the federal government has supported the use of Women Infant and Children (WIC) clinics to ensure that children are immunized. Performing lead screening in WIC clinics would dramatically improve screening rates among those children who need attention the most.[8]

On September 18, 2006, the LeadCare® II Blood Lead Testing System was categorized as a waived device under the Clinical Laboratory Improvement Amendment (CLIA). The results presented in this report demonstrate the accuracy and precision of the new CLIA waived LeadCare II blood lead testing system. LeadCare II is the only CLIA waived, portable blood lead analyzer, that is currently available.

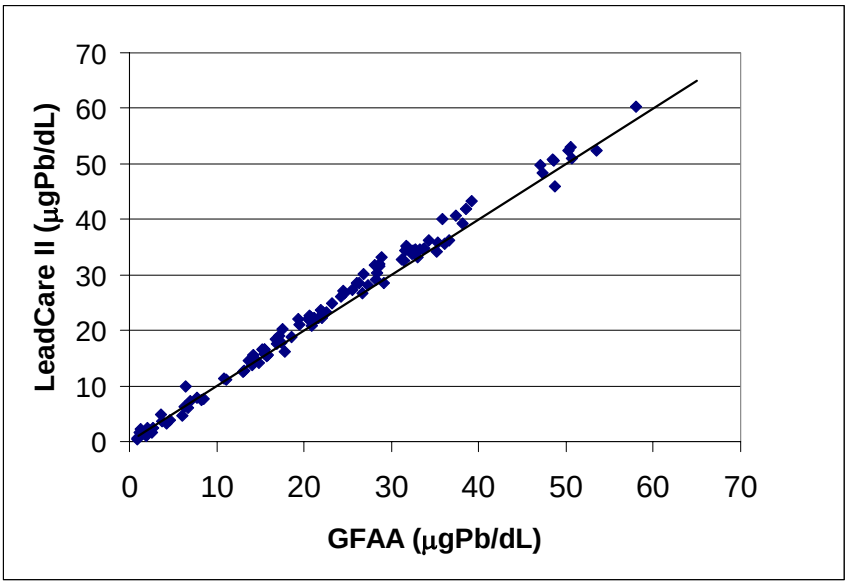
Lead analysis is performed in three simple steps. First the lab technician collects 50 µL (approx 2.5 drops) of whole blood from the patient using the capillary provided in the Test Kit. Second the 50 µL blood sample is mixed with the prepackaged treatment reagent. Once the blood sample is placed in the reagent a chemical reaction liberates the lead from the red blood cells. Third, a drop of the test mixture is placed on the sensor strip installed in the analyzer. Lead analysis begins automatically and the result is displayed three minutes later.

ACCURACY

Method Comparison

108 whole blood patient samples were analyzed by the LeadCare® II System and the Reference Method, Graphite Furnace Atomic Absorption Spectroscopy (GFAAS). Of those samples, eighty six were unspiked and twenty two were spiked with lead. A graph of the results and the pertinent statistical parameters are summarized in Figure 1.

Figure 1. Comparing results of the LeadCare II System and GFAAS.



STATISTICAL PARAMETERS
LeadCare II System vs. GFAAS Reference Method

Number of samples:	108
Slope:	1.04
Intercept:	0.12 µg Pb/dL
Correlation coefficient (R):	0.992
Standard Error of y:	1.30 µg Pb/dL
Range:	0.9 – 58 µg Pb/dL

PRECISION

The precision of the LeadCare II system was determined by testing samples at four concentration levels on six LeadCare II analyzers over twenty days. The pooled results are provided in the table below. In addition, the Within-run (WR) precision was calculated from ten replicates on the six analyzers in one day and the results are provided in Table 1.

Table 1. Precision pooled across LeadCare II analyzers.

Total Avg, µg Pb/dL	Pooled Total CV	Pooled Within-run CV	Pooled total SD	Pooled WR SD	N for total precision	N for within-run precision
5.7	12.2%	12.2%	0.64	0.64	120	60
11.0	7.6%	7.3%	0.83	0.75	120	60
22.9	5.5%	4.9%	1.26	1.08	120	60
51.7	3.5%	3.5%	1.80	1.74	120	60

CLINICAL FIELD TRIAL

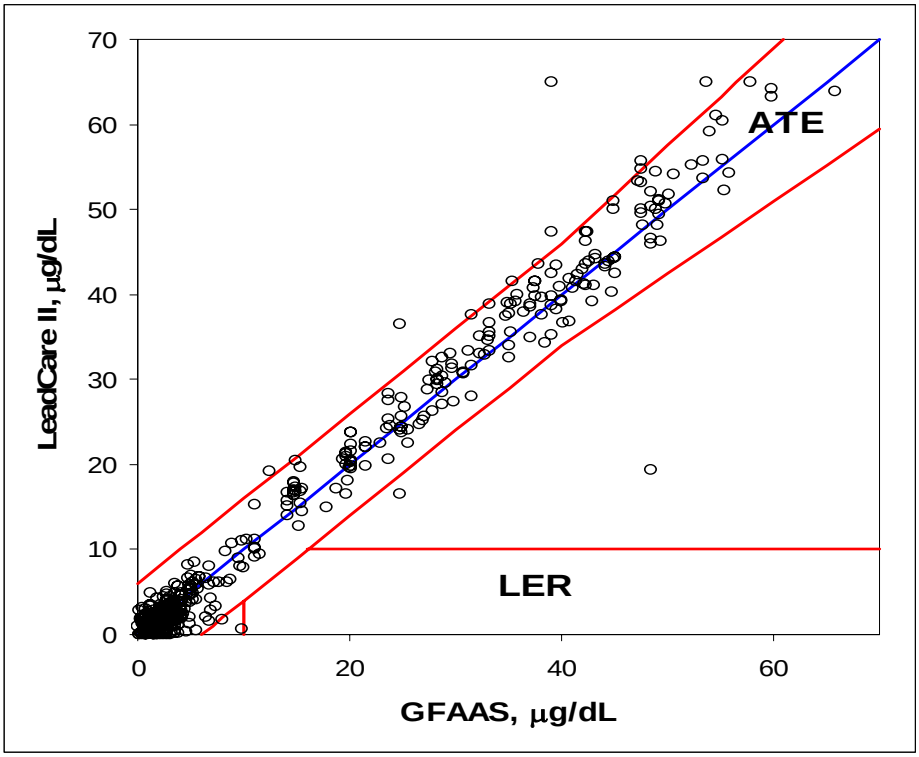
A clinical field trial was conducted at ten sites with operators who represent the intended users of the LeadCare II system. These operators were medical assistants, health outreach specialists, a diagnostic technician, and a health district office clerk. The sites were located in three different regions of the United States: five were neighborhood health centers in Brooklyn, New York, administered by Lutheran Healthcare; three were Women Infant and Children's clinics in Vermont administered by the Vermont State Health Department; and two were clinics in Chicago, Illinois, administered by the Chicago Department of Health. There was one operator at each site one except for one site which had two operators. No training on the use of the LeadCare II device was given to any of the eleven operators and they incorporated its use into their daily work flow.

Capillary and venous bloods were collected from patients for the clinical trial. Three sites collected capillary blood from fingersticks and the analyzed the samples onsite by LeadCare II and later by GFAA. Seven sites drew venous samples and split the samples three ways so that LeadCare II analysis could be conducted onsite and portions of the blood could be analyzed by GFAAS at ESA Laboratories and by the site's normal laboratory. Each site ran three patient samples per day over a ten work day period. In addition to patient samples, each site ran one spiked sample (ranging from 11-65 µg/dL) per day. These spiked samples were provided by ESA Biosciences.

During the clinical trial, 547 samples (437 patient samples and 110 spiked samples) over a two month period were analyzed at the ten sites which was consistent with the Food and Drug Administrations' 2005 Clinical Laboratory Improvement Amendment (CLIA) waiver guidelines.[9] Of the 547 samples run on LeadCare II, 516 or 94.3% of the samples, were analyzed by GFAAS, considered a Type A Comparison Method. Samples that could not be analyzed by GFAAS were due to clotted samples or a procedural error.

A graph and statistics of the clinical field trial results are shown in Figure 2. Over the entire range, greater than 95% of the samples fell within the Allowable Total Error (ATE) zone. Any sample in the LER zone indicates a failure to properly identify hazardous blood lead concentrations and is dangerous. In the study, *no samples* were in the LER zone (0% with an upper bound of 95% confidence interval of 0.5%).

Figure 2. Comparison of LeadCare II clinical field trial results to GFAAS.



STATISTICAL PARAMETERS
LeadCare II System vs. GFAAS Reference Method

Number of samples:	516
Slope:	1.04
Intercept:	-0.46 µg Pb/dL
Correlation coefficient (R):	0.976
Standard Error of y:	2.76 µg Pb/dL
Range:	0.2 – 65.9 µg Pb/dL

The clinical study demonstrated that after reading only the test instructions, operators were able to obtain results on the LeadCare II that were as accurate as those obtained on GFAAS using the following performance limits: Allowable Total Error (ATE) defined as (GFAAS result ± 6 µg/dL) for GFAAS results ≤ 40 µg/dL and (GFAAS result ± 15%) for GFAAS results > 40 µg/dL[10]. The percentage of samples over the entire range that fell within the ATE zone was 97.9% (505/516) with a lower bound of 95% confidence interval of 96.6%, see Table 2.

Table 2. LeadCare II Clinical Trial Results.

Range of GFAA values (µg Pb/dL)	Total Number of Samples	Number of Samples within ATE zone	Percent of Samples within ATE zone
0 to 10.0	314	312	99.4%
10.1 to 40.0	138	132	95.7%
40.1 to 65.0	64	61	95.3%
0 to 65.0	516	505	97.9%

CONCLUSION

The LeadCare II Blood Lead Testing System is a viable method for screening children for elevated blood lead levels. Instrument performance was evaluated by comparison to a common Reference Method (GFAAS) and the LeadCare II system proved to be accurate, precise, and simple to use in the hands of people unaccustomed to performing laboratory tests. The demonstrated ease of use in the clinical trial and the portability of LeadCare II will play an important role in enabling the effective screening of at-risk children by Public Health Clinics, Physicians Office Labs, and Occupational Health Departments.

REFERENCES

1. Lead Exposure in Children: Prevention, Detection, and Management, PEDIATRICS Vol. 116 No.4 October 2005, pp. 1036-1046 AAP Policy.
2. Recommendations for Blood Lead Screening of Young Children Enrolled in Medicaid: Targeting a Group at High Risk, Feb 2000.
3. GAO Report – Lead Poisoning, Federal Health Care Programs Are Not Effectively Reaching At-Risk Children – January 1999.
4. Kaiser Commission on Medicaid Facts, October 2005.
5. US Government Accountability Office, *Stronger Efforts Needed to Ensure Children's Access to Health Screening Services,* Pub no GAO-01-749 (Washington DC: GAO, July 2001).
6. An Ounce of Prevention: Best Practices for Increasing Childhood Lead Screening by New York's Managed Care Plans.
7. Preventing Lead Exposure in Young Children: *A Housing Based Approach to Primary Prevention of Lead Poisoning,* Recommendations From the Advisory Committee On Childhood Lead Poisoning.
8. GAO Report – Lead Poisoning, Federal Health Care Programs Are Not Effectively Reaching At-Risk Children – January 1999.
9. Draft Guidance for Industry and FDA Staff: *Recommendations for Clinical Laboratory Improvement Amendments of 1988 Waiver Applications,* FDA, Center for Devices and Radiological Health – Released September 7, 2005.
10. Recommendations for Blood Lead Proficiency Testing - Occupational Safety and Health Administration of U.S. Department of Labor (OSHA).