Anatomy of the LeadCare Product Recall

ESA LeadCare Analyzer

- A portable device for measuring blood lead (BPb) levels.
- Based on Anodic Stripping Voltammetry (ASV).
- Uses disposable screen-printed electrodes.
- Requires blood to be “treated” with a reagent that decomplexes lead bound to proteins.
- Takes around 3-4 minutes per analysis.

ESA LeadCare

- Calibration using an electronic button.
- Buttons are specific to each batch of sensors.
- Blood specimens are treated with reagent for 1 minute.
- Treated blood deposited on the sensor.
**ESA LeadCare**

- **Advantages:**
  - Moderately complex but easy to use.
  - Dr’s office use
  - Rapid results (3-4 m)
  - Low cost device (~$2K)
  - $7 a test
  - Can operate @ 9V

- **Limitations:**
  - Blood must be fresh (<24 hrs old)
  - Cannot refrigerate blood
  - Response is affected by glutathione
  - Sensor lots may vary
  - Temperature sensitive

**WI Proficiency Program**

- Bureau of Maternal and Child Health sponsors the PT program
- Our cows are dosed with lead, so it is biologically bound
- The samples are aliquoted and stored frozen until shipment
- Mailed to participants, who analyze the samples and report results back, which are then graded

**Target values are determined by a group of referee laboratories**

- LeadCare targets are determined by participant mean
- Currently there ~600 labs in the program, about half are LeadCare
  - ~40 International labs

**Offer two types of Programs**
- Regulatory Program
- Monthly Blood Lead Program
Number of Labs Reporting Blood Lead

- **Lead Care**
- **Total participants**

Date

- 7/97
- 1/98
- 7/98
- 1/99
- 7/99
- 1/00
- 7/00
- 1/01
- 7/01
- 1/02
- 7/02
- 1/03
- 7/03
- 1/04
- 7/04
- 1/05
- 7/06

**LeadCare Recall Chronology**

- In May 1997, data\(^1\) was presented comparing the LC prototype with a reference method. It was concluded that it was accurate for screening children.
- In September, the LeadCare is commercially introduced.
- In October, LeadCare users begin to enroll in the WI PT Program.


**LeadCare Recall Chronology**

- It was expected that the samples would exhibit a positive bias, relative to other methods.
  - Due to specimen prep and absence of glutathione.
- This positive bias was observed in early PT events.
- Consequently, in December 1997, it was decided that LeadCare results should be evaluated as a separate group.

**LeadCare Recall Chronology**

- In January 2000, our enrollment had grown from 9 to approximately 100 and the positive bias had disappeared.
- The LeadCare now exhibited a low bias compared to other methods.
- Despite several cooperative efforts by ESA and WI, the reason for this trend was not determined.
In June 2001, Taylor, Jones, et all, report that a comparative study of occupationally exposed adults demonstrated a modest positive bias for the LC compared to a referee method.


In August 2004, the Blood Lead PT program administered by NY State reports a low bias in LeadCare results compared to other methods.

- NY provides fresh whole animal blood
- Directly compare LeadCare with other methods

- Failure rates of 69% and 38% for the previous two PT events
  - Failure rates had previously been below 10%

In November, there continues to be a low bias and NY gave the directive to report only qualitative results ($\geq 10 \text{ µg/dL}$ or $<10 \text{ µg/dL}$)

---

**Is the Bias Real?**

- Artifact of Animal Blood?
- Artifact of the processing?
LeadCare Recall Chronology

- In December 2004, WSLH and ESA initiate a cooperative evaluation study using fresh human blood from occupationally exposed workers.
- Three sensor lots were examined and all three demonstrated a low bias.

What happened next?

- ESA reviewed data and requested additional studies…
- WSLH conducted a second study, using fresh human blood from exposed workers:
  - The blood was placed in reagent at WSLH and shipped to ESA for analysis.
  - A fourth sensor lot was used.
Spring 2005

- WI shared data with representatives from NY and CDC seeking comment
- Contacted Bureau of Maternal & Child Health (MCH) about the bias and shared data
  - Conference call was held with MCH, ESA, WI, and CDC to discuss issue

Spring 2005, cont’

- Correspondence from the CDC, that more data is needed, especially since the results were from occupationally exposed adults and not children
- Noted a CDC publication regarding positive bias on adult blood

Spring 2005, cont’

- Beginning in April we started asking our participants in the PT program to provide us with their sensor lot code for further investigations
- There were 2 labs using a new lot, and their results were higher than the other LeadCare labs and the referee targets
- Shared this data with ESA

Spring 2005, cont’

- May 3, WI receives the newest lot of LC sensors to evaluate.
- ESA indicates that this new lot should read higher than other lots on the PT specimens, but not on patient specimens
  - This is attributed to “different glutathione sensitivity”
Spring 2005, cont'

- May 12, Testing of the new lot is completed. And as anticipated, results on the PT specimens were higher.

- May 12, WI concludes that the bias is real and recommends that LeadCare users should be notified and contacts MCH.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Lot ESA</th>
<th>Referee</th>
<th>Lot USG</th>
</tr>
</thead>
<tbody>
<tr>
<td>0602-01</td>
<td>12.6</td>
<td>1.2</td>
<td>1.7</td>
</tr>
<tr>
<td>0602-02</td>
<td>12.6</td>
<td>1.2</td>
<td>1.7</td>
</tr>
<tr>
<td>0602-03</td>
<td>26.9</td>
<td>19.8</td>
<td>26.7</td>
</tr>
<tr>
<td>0602-04</td>
<td>10.0</td>
<td>10.0</td>
<td>10.1</td>
</tr>
<tr>
<td>0602-05</td>
<td>10.0</td>
<td>10.0</td>
<td>10.1</td>
</tr>
<tr>
<td>0602-06</td>
<td>29.9</td>
<td>29.9</td>
<td>30.3</td>
</tr>
<tr>
<td>0602-07</td>
<td>14.8</td>
<td>12.3</td>
<td>14.5</td>
</tr>
<tr>
<td>0602-08</td>
<td>31.0</td>
<td>21.0</td>
<td>27.0</td>
</tr>
<tr>
<td>0602-09</td>
<td>31.0</td>
<td>21.0</td>
<td>27.0</td>
</tr>
<tr>
<td>0602-10</td>
<td>22.0</td>
<td>22.0</td>
<td>27.0</td>
</tr>
<tr>
<td>Average</td>
<td>Targets</td>
<td>Average</td>
<td></td>
</tr>
</tbody>
</table>

Spring 2005, cont'

- May 13, Contacted by ESA that they were voluntarily issuing a recall.

- The recall was prompted by the studies with WI and additional in-house testing.

Spring 2005, cont'

- May 20, WI receives the official recall notice issued by ESA.

- The notice states that a low bias of 26% was detected for sensor lots dating back to September 2003.

- 8 lots were recalled.

- Recommendation to retest children with lead levels exceeding 6 ug/dL.
Consequences

- Based on the recommendation to retest children with leads >6 μg/dL:
  - State of MA, ~6000 results were affected
  - State of CA, ~100,000 suspect results, ~2% will need to be retested
  - Nationally …

Notification

- WI agrees to provide a mailing to PT participants that includes the recall letter
- WI will also monitor the sensor lots reported, and provide information back to ESA

Performance

- Data obtained on the new test kit lots demonstrate much improved comparability on fresh human blood
- Absence of significant bias in the NY program
- Results in the monthly WI program also show a disappearance of the negative bias
Recent Developments

- Based on recent data on the new sensor lots, NY lifted their qualitative reporting restriction on November 21st.
- The official closing of the recall by the FDA was anticipated in November 2005.
- In WI, the issue in the PT program was resolved by August.

What Did We Learn?

- Value of PT extends beyond the evaluation of individual laboratories.
- Changes in performance can provide evidence of widespread analytical issues.
- Cooperation between the manufacturer and the PT providers facilitated the investigation and resolution of the problem.
What's on the Horizon?
- Development of a new LeadCare analyzer that will be ‘waived’
- Similar to the current LeadCare, but will not have to quantitatively measure the blood
- By being waived, this instrument would not have to participate in PT

And the bias problem?
- Rooted in human error during the calibration process and not a defect in the sensors themselves
  - An absence of glutathione
- Blood that was used to calibrate was the same as what WI uses in its PT program
  - Need to add glutathione to our blood