

## **Lysosomal Storage Disorder Screening**

### Implementation Progress in Missouri to Date

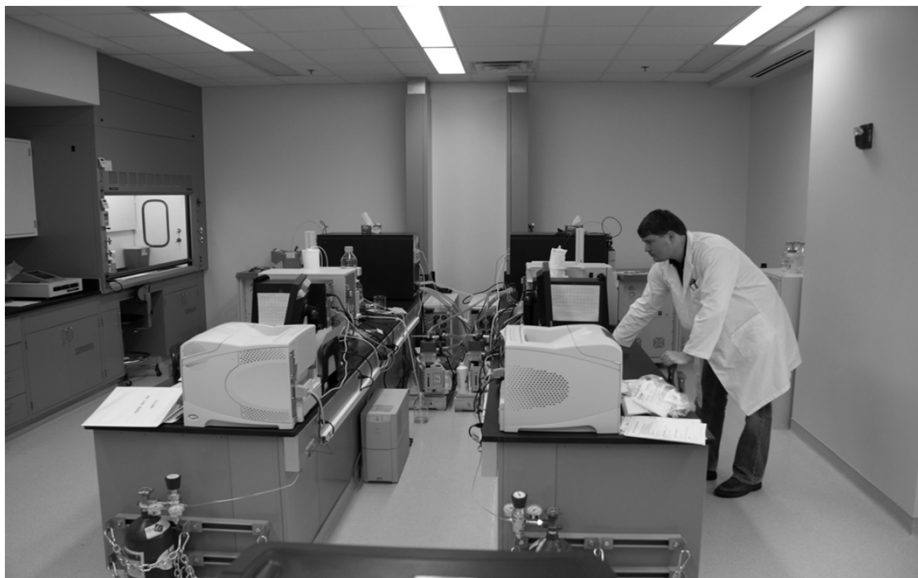


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Heartland Genetics and Newborn Screening Collaborative  
Annual Conference; St. Louis, MO; October 5, 2012

## **Choosing the Testing Method**

- Only two choices were available for high throughput: MS/MS and Digital Microfluidics.
- What are the start-up costs?
- State fiscal climate was extremely limiting:
  - No newly created FTE's allowed
  - A freeze on increasing "fees" except in a few situations (Big Government Get Off My Back Act).
  - Fee increase would take over two years to implement and even longer to make a difference.
- Lab space and retrofitting limitations

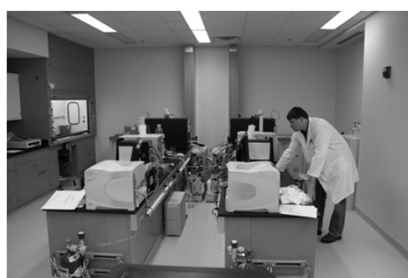
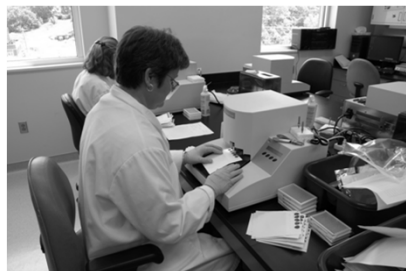
## MS/MS System



## MS/MS System: 21 Instruments!



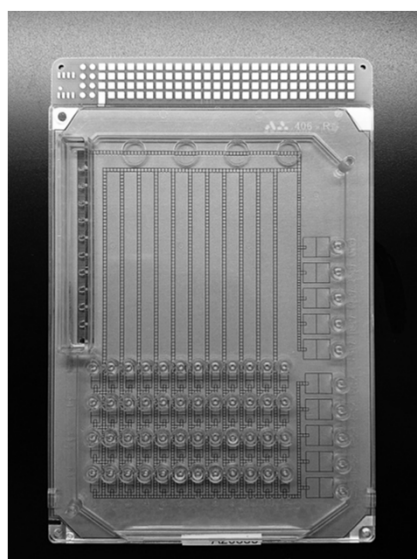
## Staff and Lab Space Already Stretched



## Digital Microfluidics Platforms from Advanced Liquid Logic (ALL)



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## Workflow for LSD Testing in MSPHL



### Punch DBS samples

(15 min per 96-well plate)  
Single punch for 4-plex assays.



### Extraction

(30 min at RT)  
Load filler fluid in cartridges. Thaw reagents during extraction.



### Loading

(6-10 min per machine)  
Load samples (1.6 $\mu$ L), reagents (6.5 $\mu$ L) and stop buffer in each cartridge.



### Machine run time

(2.5 h for 5-plex assay)  
After 2.5h remove the cartridge from the instrument and get ready for next run.



- 2 scientists currently working on 2 work stations of 8 instruments
- 48 sample wells assayed per instrument
  - 10 controls (2 blanks, 4 calibrators, 2 low controls and 2 medium controls)
  - 38 patient samples
- Sample punch to enzymatic activity results in <4 hrs

## Implementation Plan

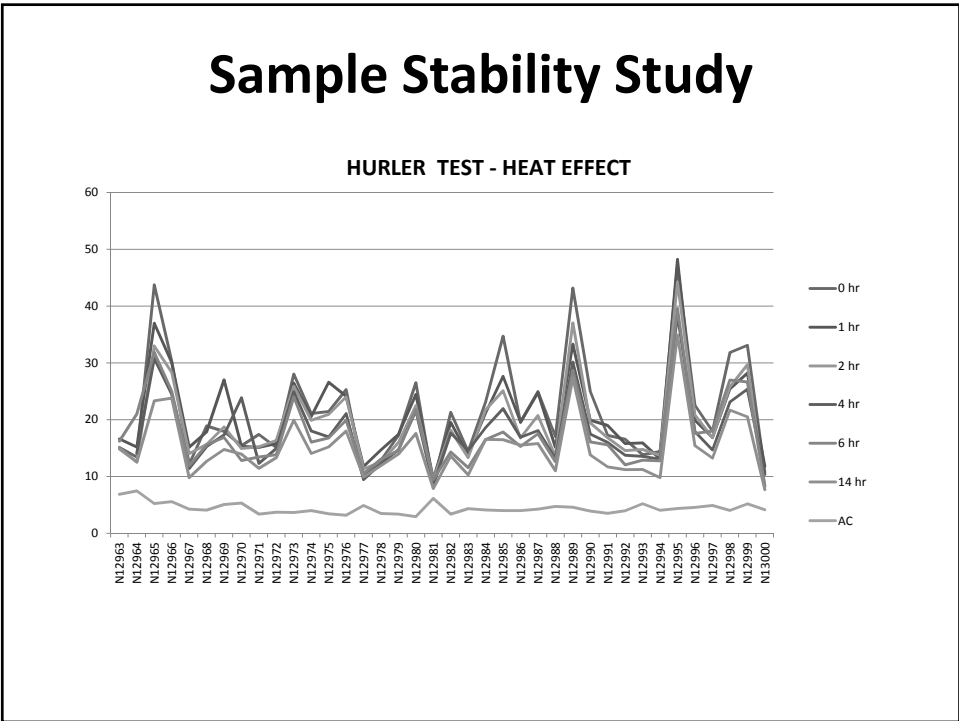
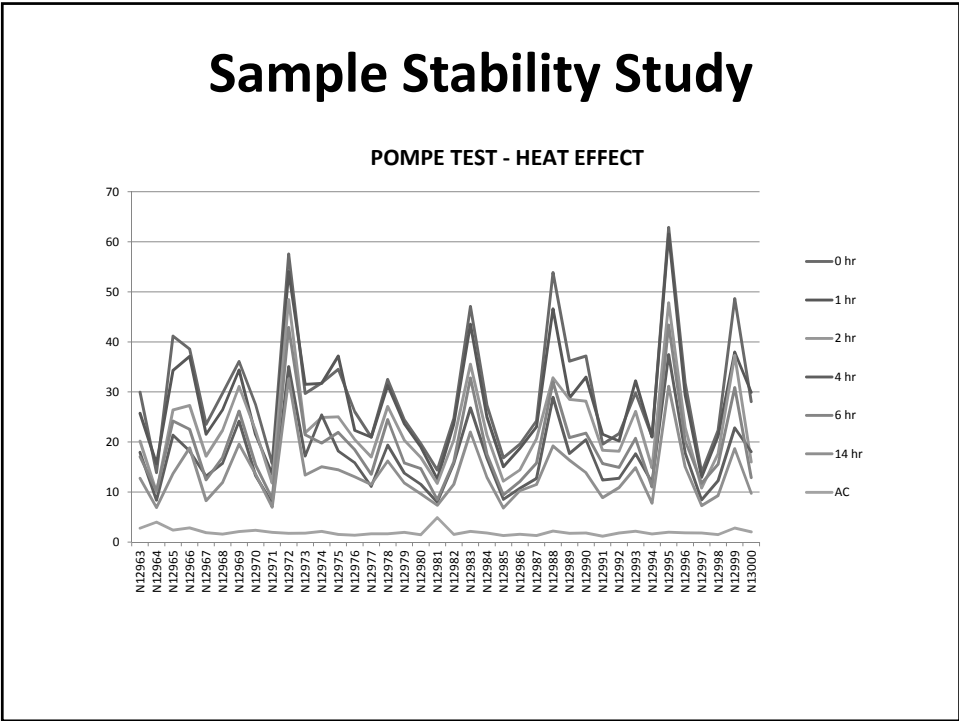
- Installation
- Training
- Familiarization
- Validations
- Pre-pilot phase (data collection on blinded samples)
- Pilot Phase (statewide testing with referrals)
- Live Testing with reporting on all NBS lab reports

## **LSD Acronyms**

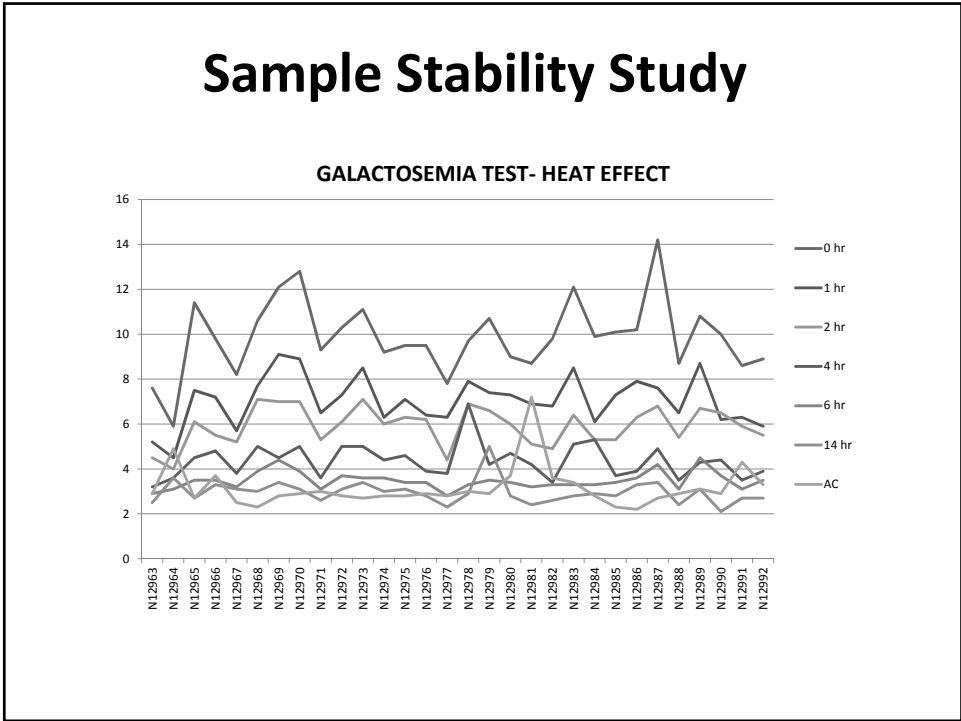
- GAA = Pompe
- GBA = Gaucher
- GLA = Fabry
- IDS = Hunter
- IDUA = Hurler
- GALC = Krabbe
- Niemann-Pick = ?

## **Validation of New Methods**

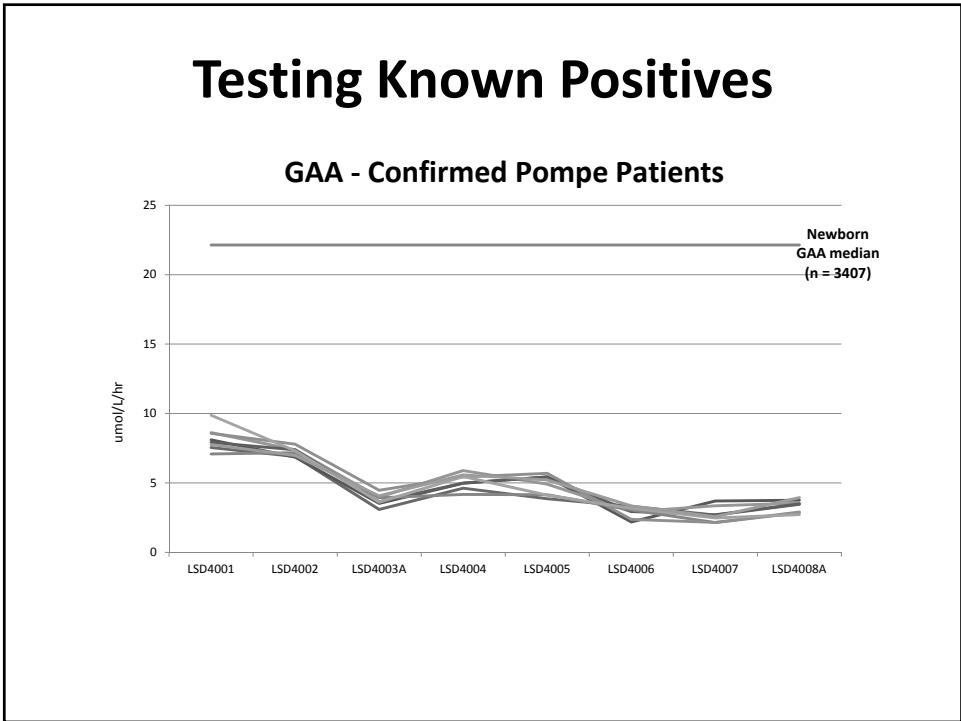
- Accuracy/Sensitivity – Using known positives, quality control and proficiency test samples.
- Precision/Specificity – Within run, between runs, between different reagent lots.
- Linearity/Limit of detection – Consistency from high to low levels of the detection range.
- Instrument matching – to maintain same cutoffs
- Carryover
- Testing interferences – Health status, age of baby, etc.



# Sample Stability Study



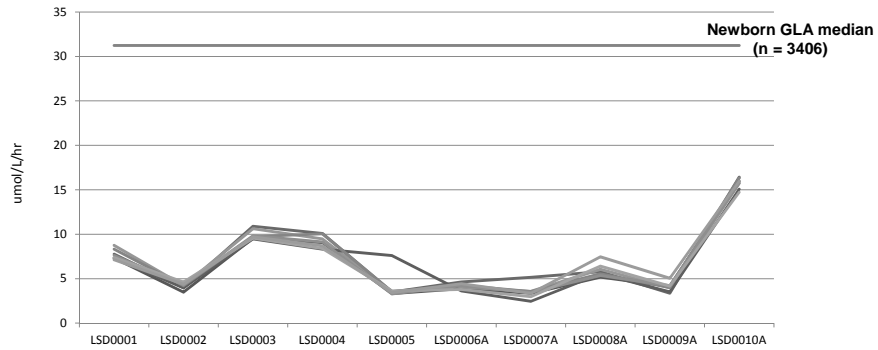
# Testing Known Positives





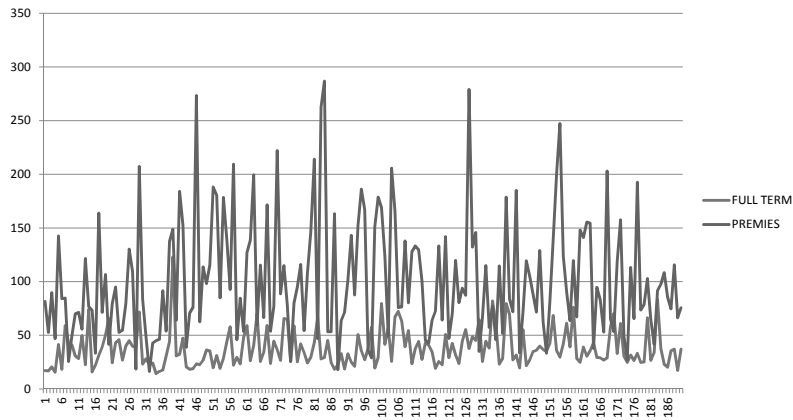
# Testing Known Positives

## GLA - Confirmed Fabry Patients



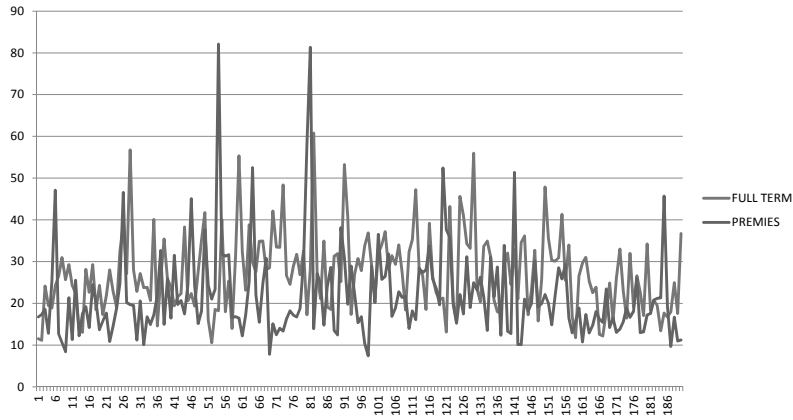
# Health Status Effect

## GLA of Full-term vs Premies



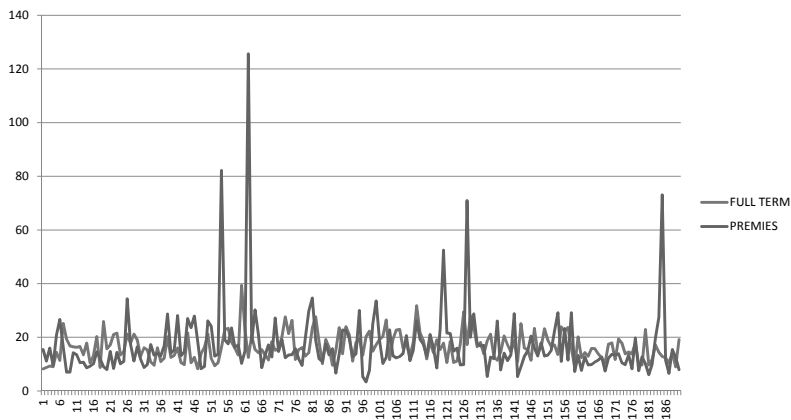
# Health Status Effect

## GAA of Full-term vs Premies



# Health Status Effect

## GBA of Full-term vs Premies



## **Progress to Date**

- Have conducted many validation experiments and are utilizing StatisPro software from CLSI.
- Have tested around 13,000 QC and CDC samples.
- Have tested over 27,000 de-identified patient samples.
- Have conducted sample exchanges with Mayo.
- Have confirmed with 3 Pompe cases diagnosed clinically and 1 Gaucher carrier.

## **July 2012 Implementation Challenges**

- Krabbe and Niemann-Pick testing delayed one year for microfluidics assay development.
- Krabbe screening being conducted through New York since August 22, 2012.
- Statewide pilot for Pompe, Gaucher, Fabry and Hurler delayed 6 months for an upgrade in the microfluidic cartridges.
- Hunter screening delayed one year for reagent development.

“Obstacles are those frightful things you see when you  
take your eyes off your goals.” — Henry Ford

**Thank You**