



The Michigan Experience with Screening for SCID in Newborns: Preparations & First 30 days

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This presentation will include:

- **Key Milestones for implementation of SCID screening.**
 - **Michigan Senate Bill 794**
- **Brief Description of Highlights TREC/B Actin Duplex Assay.**
- **Summary of Data from Method Validation and First 30 days of Newborn Screening.**



Michigan Senate Bill 794

- In 2006, MI SB 794 created a 10 member NBS Quality Assurance Advisory Committee.
- Submit a written report annually to MDCH on appropriateness of list of conditions, recommendations on changes.
- Report shall include recommendation on increase or decrease of the fee.
- If not rejected by MDCH within 30 days, moves to Senate & House committees that oversees PH issues.
- If not rejected by Legislative committees within 45 days, considered “approved” by Legislature and takes effect within 6 months.



Important Milestones for SCID Screening in Michigan

- **SCID multi-disciplinary advisory group meets June 2010 (Dr Secord, Chair)**
- **NBS QA Advisory approves adding SCID to the Michigan NBS panel and sends letter to MDCH Director (Oct 2010)**
- **“Approved” by legislature January 2011.**
- **Trainings@ CDC (October 2010) & @ WI (March 2011)**
- **Ep Motion 5075 (December 2010) & ABI 7900 HT (February 2011) received in laboratory.**



Preliminary Studies cont'd.

- TREC & B-Actin plasmids rec'd, transformation, characterization completed to provide a reliable source of calibrators (April – May 2011).
- Preliminary Experiments & Method Validation (June – August 2011)
 - DBS don't stick to Ep Motion pipette tips
 - Ep Motion used to dispense Qiagen solutions 1 & 2
 - TREC/ β Actin duplex assay used to assay ~ 5300 DBS from MI, true positives, CDC specimens in 384 well format.
- Quarterly meetings with SCID medical advisory in 2011 with 3 referral centers.
- Begin SCID screening October 1, 2011



Laboratory Goal

- It was already shown by WI, MA NBS that the measurement of TRECs can detect infants with SCID & related disorders using qPCR.
- The Michigan goal was to build on these efforts and:
 - To provide calibrators, controls and other reagents for routine screening
 - To provide a working assay with automated DNA extraction in a duplex assay format
 - Begin screening for October 1, 2011

TREC- β actin duplex assay

- DNA extraction uses Qiagen solutions 1 & 2 in 3 step process.
- DNA extraction & PCR 384 well setup performed on Ep Motion 5075 with limited user intervention.
- TREC & β actin calibrators prepared in house.
- PCR product- 88 base pairs.
- Probes and forward primer same as Baker et al.

Summary of Method Validation Data (n= 5307)

- From population studies, Mean TREC values = 291, Median = 222 (copy #/ul blood).
- TREC Current cutoff: 30 copy #/ul blood.
- 99.8% of specimens screened normal.
- Range of TREC values for 13 true positives cases: undetectable-11.
- 7 false positives, 5 inconclusive from population studies.
- CDC specimens (MPES, cord blood & HeLa cell calibrators, in house controls,) assisted with validation and cutoff determination.

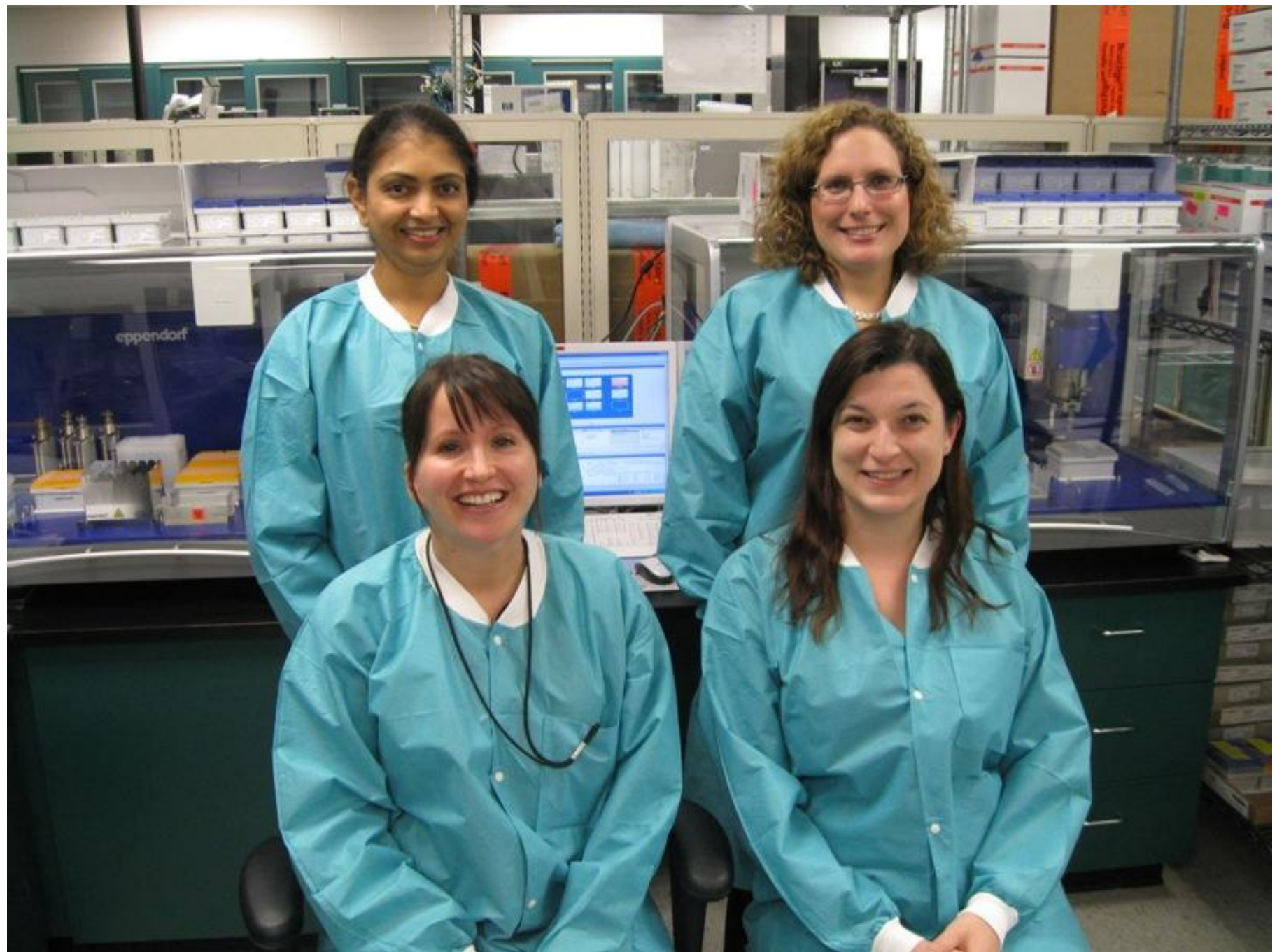
Summary of First 30 Days of SCID Screening

- **99.8% of specimens screened normal (n=9889)**
- **11 screen positives(5 confirmed normal, 6 pending);
10 of 11 from NICU.**
- **9 inconclusive (9 normal on repeat); 1 of 9 from
NICU.**



Summary

- Michigan began offering SCID screening in its NBS panel.
- We have implemented a partially automated method for DNA extraction and PCR in a duplex assay format.
- Our positive rate is about 0.2 %. We hope to reduce false positives by developing separate TREC cutoffs for premature, LBW infants in the NICU.





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