# CDC's Role in the Implementation of Newborn Screening Pilot Programs

## *Activities of the Newborn Screening and Molecular Biology Branch*

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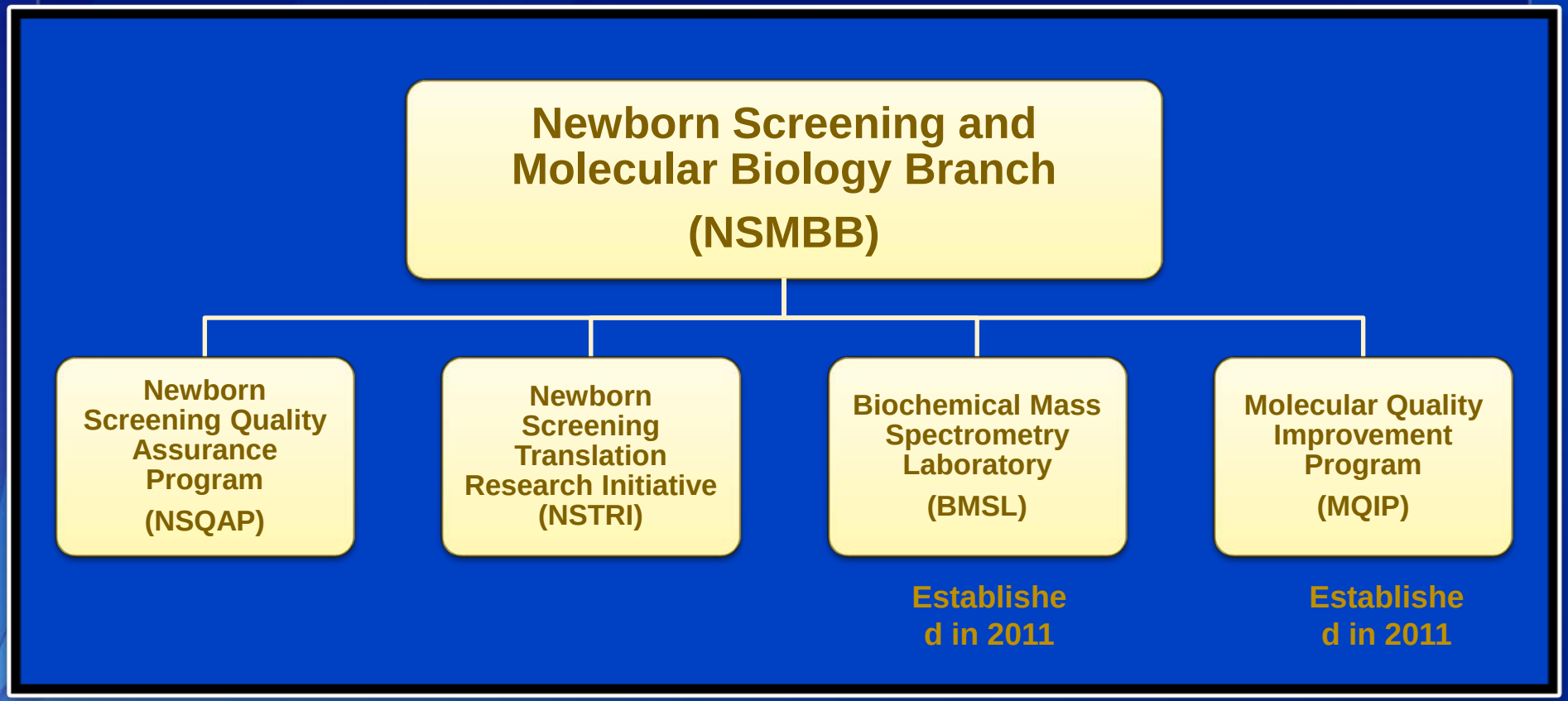
# Newborn Screening and Molecular Biology Branch

***Goal: Assure the early and accurate laboratory detection of heritable disorders in newborns through dried blood spot testing***



# CDC Funding Opportunities for SCID

- **Funding and administration of FIRST public health pilot studies of newborn screening for SCID**
  - **Public Health Labs: Massachusetts and Wisconsin (~ $500K/yr)**
  - **Three Years: Fall 2008, Fall 2009, Fall 2010**
- **Funding and support of SCID Newborn Screening pilot study among Native Americans**
  - **Pilot studies: Fall 2008, Fall 2009 (~ $100K/year)**
- **Additional 2 year SCID NBS implementation funding**
  - **Fall 2011, Fall 2012 …. Michigan and Minnesota (~$400K/yr)**
  - **Fall 2013, Fall 2014 …. Oklahoma, Virginia and Georgia (~$200-$300K/yr)**
  - ***Fall 2015?***

# SCID NBS Funding Opportunities

- **Early Research Pilot Objectives:**
  - **Develop, Evaluate, and/or Improve newborn bloodspot screening tests for SCID** to increase sample though-put, positive predictive value, multiplexing capacity
  - **Develop and/or evaluate second tier tests** to confirm primary tests and reduce false-negative results
  - Develop and/or evaluate novel approaches for **data analysis and statistical algorithms** that can improve the predictive values of primary SCID NBS tests
  - Increase the pool of laboratory scientists with **knowledge and skill** in conducting NBS for SCID
  - Provide **training for the public health community** ….. to foster their integration into the standard of care for communities

# CDC activities that support sustainability of Pilot Programs and Implementation of Screening for Newborn Conditions

# 1. Newborn Screening Quality Assurance Program supports quality testing

***The only comprehensive quality assurance program using dried-blood spots***

- ❑ Quality Control Materials
- ❑ Proficiency testing
- ❑ Filter paper evaluation
- ❑ Translational Research

Preparation of whole blood pools

Reference Material Production

Certification of Blood Spots

Packaging and Shipment to Participating Labs

# Development of Quality Control Materials for new programs

- Quality Control materials: provide a high degree of confidence that testing results are ACCURATE for the batch of samples tested

- Quality Control materials  monitor method performance over time
  - Document trends in method performance
  - Identify problems so that corrective actions can be taken quickly

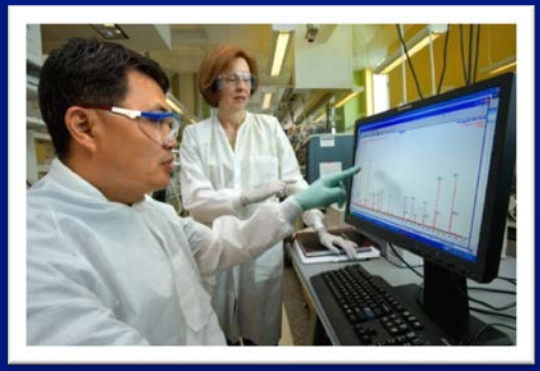
- *CDC QC* – EXTERNAL QC
  - Supplemental materials, not for every day use
  - Should be run periodically to assess method
  - QC Data is evaluated 2 times per year

Source:  http://www.cdc.gov/labstandards/nsqap.html

# Proficiency Testing Dried Blood Spot Materials for Newborn Screening

- **Proficiency Testing: Lab is evaluated for its ability to get same results on a set of samples**
  - Assessment at one point in time
  - Similar to patient testing (or as close as we can get it)

- **CDC Proficiency Testing Programs**
  - 3 times per year for US and International participants
  - One-month data turnaround to receive results



Reference: https://wwwn.cdc.gov/nsqap/public/default.aspx

# NSQAP Analyte Implementation Timeline

- 1978 - Congenital hypothyroidism (T4, TSH)
- 1980 - Phenylketonuria (Phe)
- 1988 - Galactosemia (TGal); HIV antibodies
- 1990 - Congenital Adrenal Hyperplasia (17-OHP)
- 1991 - Sickle Cell Disorders
- 1992 - Maple Syrup Urine Disease (Leu, Val)
- 1994 – DNA Confirmatory methods for Hb S, A, C, E D
- 1995 - Homocystinuria (Met)
- 1997 - Biotinidase; Cystic fibrosis F508del
- 2001 - MS/MS Analytes (Tyr, C3, C4, C8, C14, C16); GALT
- 2002 - Cystic Fibrosis (IRT); Cit, C6, C10
- 2003 – C5, C5DC
- 2005 - *Toxoplasmosis gondii* PT
- 2006 - 2nd tier Congenital Adrenal Hyperplasia by MS/MS (17-OHP, androstenedione, cortisol, 11-deoxycortisol, 21-deoxycortisol)
- 2007 - Cystic Fibrosis DNA Mutation Panel; C0, C2, C10:1, C14:1
- 2008 - Succinylacetone
- 2008 - Lysosomal Storage Disorders (Krabbe, Pompe, Gaucher, Niemann-Pick A/B, Fabry, MPS-1)
- 2009 - 2nd tier Maple Syrup Urine Disease (Alloisoleucine, Isoleucine); C5OH, C18
- 2010 – Arg, C4OH, C5:1, C12, C16OH
- 2011 – SCID (TREC); C18:1
- 2012 – Ala, C10:2
- 2013 – C18OH
- 2015 – XALD, G6PD

# NSQAP Quality Assurance Programs

- **Quality Control**
  - 17-OHP
  - T4
  - TSH
  - Amino acids, SUAC and TGal
  - Acylcarnitines
  - IRT
  - X-ALD
  - GALT
- **Proficiency Testing**
  - Hormones (T4, TSH, 17-OHP, TGal)
  - Amino acids, SUAC
  - Acylcarnitines
  - IRT
  - CF DNA
  - *Toxoplasmosis gondii*
  - Hemoglobinopathies
  - 2nd tier CAH
  - LSD
  - TREC
  - Biotinidase
  - GALT
  - G6PD*
  - X-ALD*

*starting July 2015

# Processes involved in Newborn Screening Dried Blood Spot (DBS) Production



**NSQAP prepares, certifies and distributes over 850,000 DBS each year**

**Key Point:**

**Critical that CDC be involved in early stages of any NBS condition* that is being considered for nationwide implementation**

**Development of robust QA materials is not trivial and requires iterative evaluation with early adopting programs to assess performance and to document proper certification of materials**

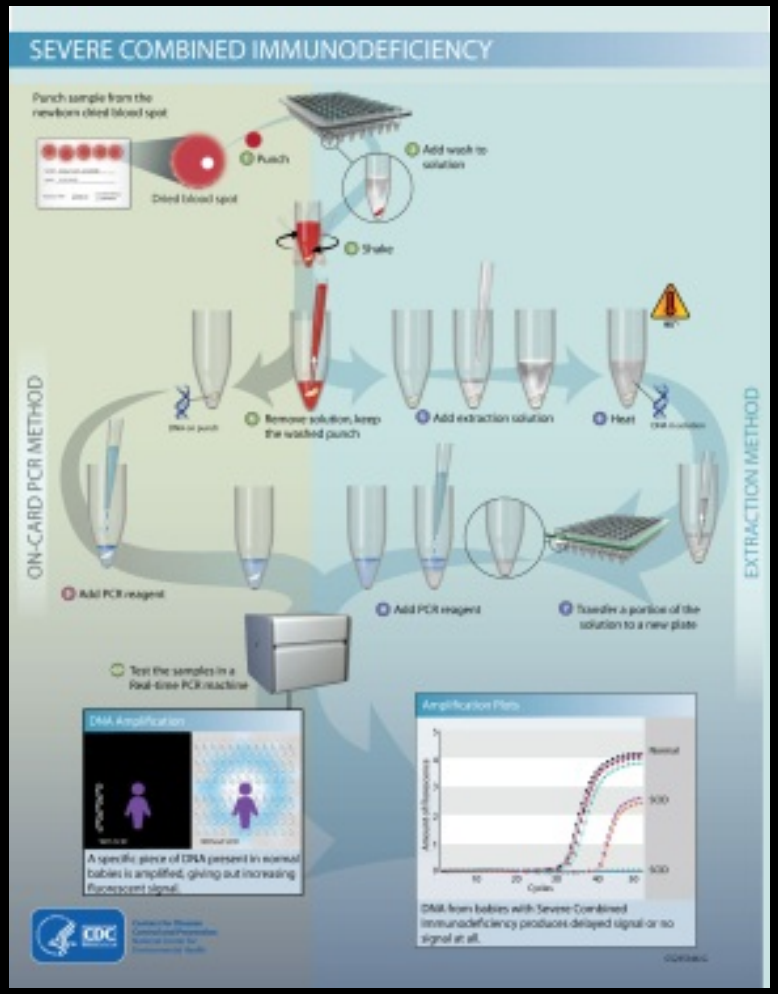
*** conditions identified through dried blood spot evaluation**

# 2. Method Development: New targets and Quality Improvement for Existing Targets

- Important to have expertise in Newborn Screening Methods
  - Evaluation of QA materials
  - Troubleshooting with State labs
  - Opportunities for training state program lab personnel

Each Laboratory within the Branch is actively engaged in method development using dried blood spots for anticipated conditions

# On-card real time PCR compared to Extracted DNA real time PCR

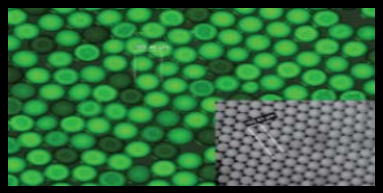



- Developed *on-card* real-time PCR TREC assay for SCID using DBS
- Development of digital PCR technology: Absolute TREC copy number

**Digital PCR: *The Next Generation of Quantitative PCR***

- Allows for absolute copy number quantification
- No standard curve needed
- Greatly improved precision over real time PCR (< +/- 10% error)
- Greater sensitivity – lower limit of quantification

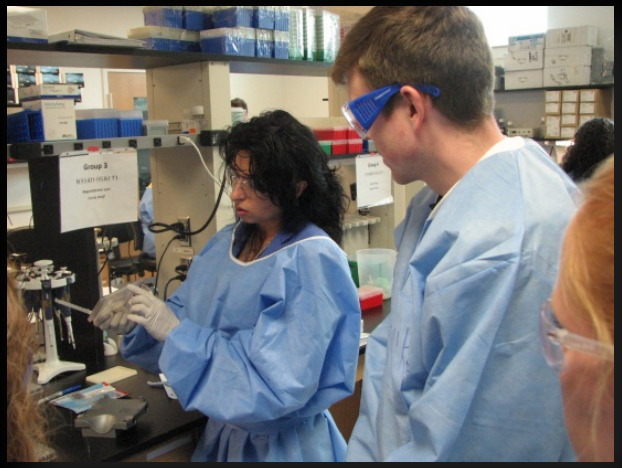
**Ideal platform for measuring calibrators and reference material**



# 3. Technical Program Support

## Provide Training and Support to Maintain Technical Expertise within NBS Labs

- National meetings
- Laboratory-based Training
- 1:1 Consultation
- Laboratory data review
- Site visits
- Website Resources



# National Meetings and Discussions

- ***National conversations give States the opportunity to share best practices and address areas of concern with Program-based solutions***

## Newborn Screening for Severe Combined Immunodeficiency: *Implementation, Challenges, and Successes*

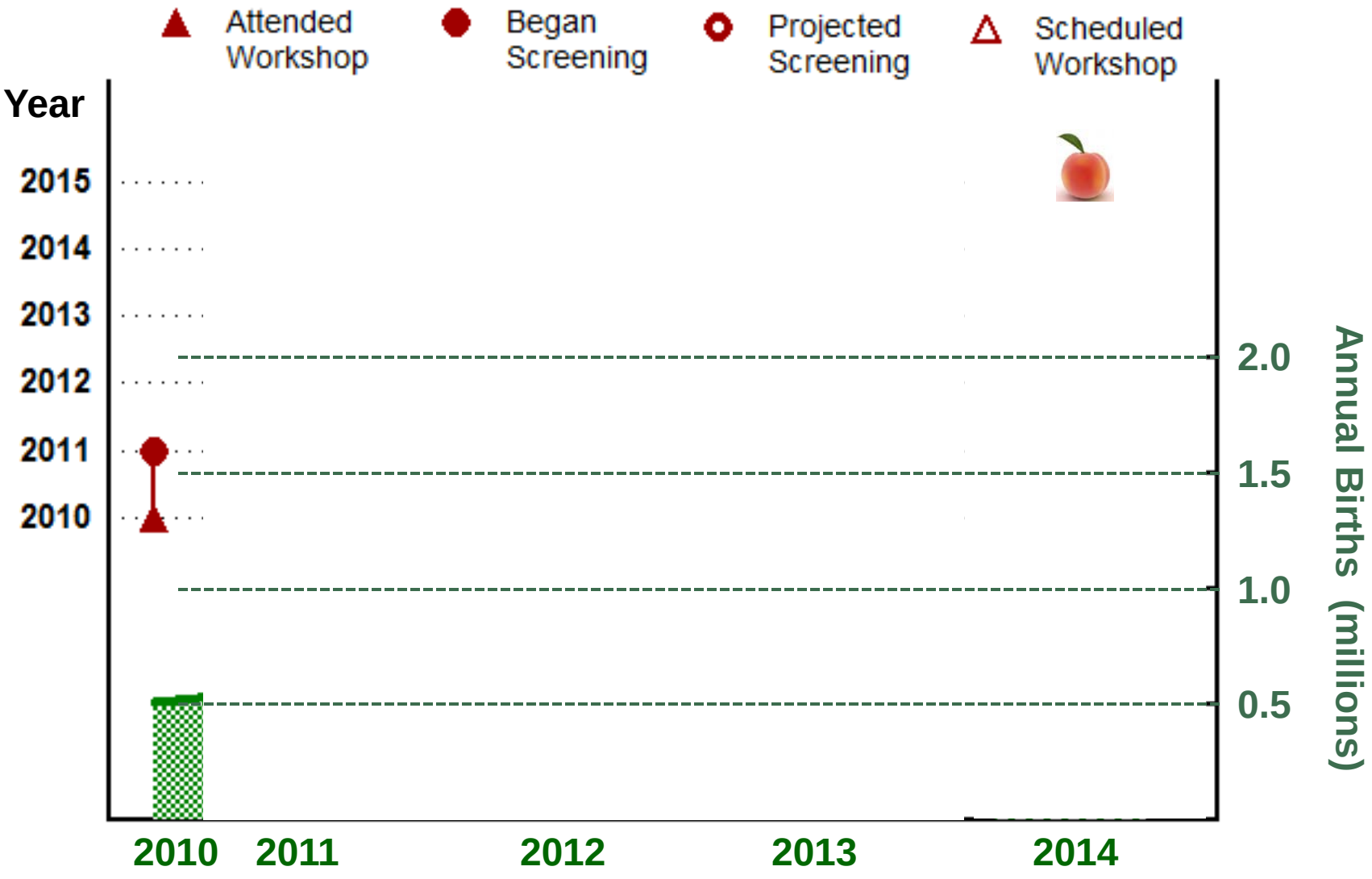
- **Outline basic information regarding SCID and its detection through the newborn screening process**
- **Describe the basic testing methodologies of SCID testing and state implementation experiences**
- **Discuss the treatment and clinical management of patients with SCID**

**Target Audience:**

**State Newborn Screening Laboratorians**
**Newborn Screening Follow-up Program Personnel and Physicians**
**Newborn Screening Stakeholders**

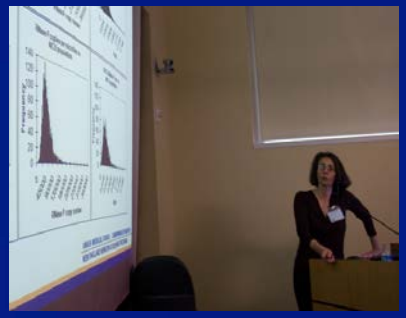
***Hosted by APHL and NNSGRC in October 2010**

# CDC SCID Workshops for Public Health Laboratories



# Workshops and Technical Meetings

- Scientific Workgroups and meetings addressing technical details of methods implementation
- Workshop on SCID testing and TREC Reference Materials
- Public Health Laboratory representatives from CA, CT, GA, MA, MN, WI, NY, TX



# Laboratory-based Courses: Using Mass Spectrometry and Molecular Biology platforms

- In a climate where there may be high staff turnover, it is important to provide opportunities to support staff competency
- Intensive lectures and hands-on laboratory training
- Offered once or twice a year as needed

# Site Visits to Evaluate Laboratory Workflow and Assist with Troubleshooting

## NBS Molecular Assessment Program (MAP)

- Helps laboratories gauge current quality assurance practices and identify potential improvements to testing quality or efficiency
- MAP can provide support for determining how to fit molecular testing into the laboratory given existing program resources and application needs.
- The MAP guidance covers numerous laboratory processes including documentation, workflow, assay validation and results reporting.
- Feedback from the visit is provided in an exit discussion and a confidential written report to the program.

*MAP: Non-regulatory site visit of molecular biologists from CDC and State Public Health newborn screening programs. 14 visits to date.*

# 4. Support of NBS Laboratory Practice through Partnerships

- CDC has a cooperative agreement with APHL that supports:
  - Newborn Screening and Genetics in Public Health Committee
  - QA/QC subcommittee
  - NBS Molecular Subcommittee
  - Other ad hoc workgroups and initiatives
- Partnerships enable:
  - Guidance on policies, development of white papers, position statements
  - Facilitate training opportunities through courses, workshops, webinars, 1:1 training, on-line website resources

# Thank you for your attention!

## *Newborn Screening*

***Saving* Lives.**

***Promoting* Healthier Babies.**

***Protecting* our Future.**

**For more information please contact Centers for Disease Control and Prevention**
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