Overview of Newborn Screening Laboratory Processes and Quality Management

Scott M. Shone, PhD

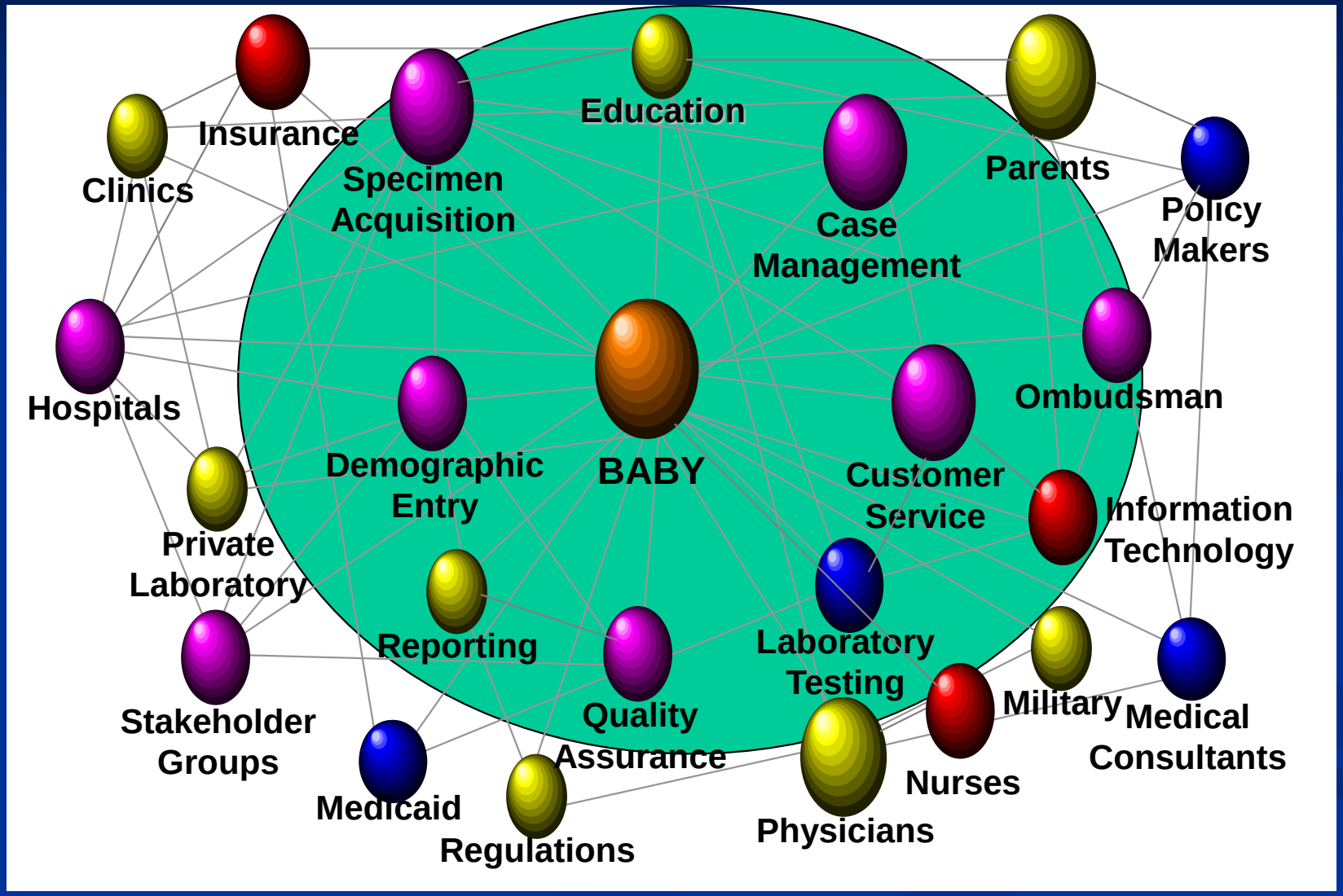
Program Manager

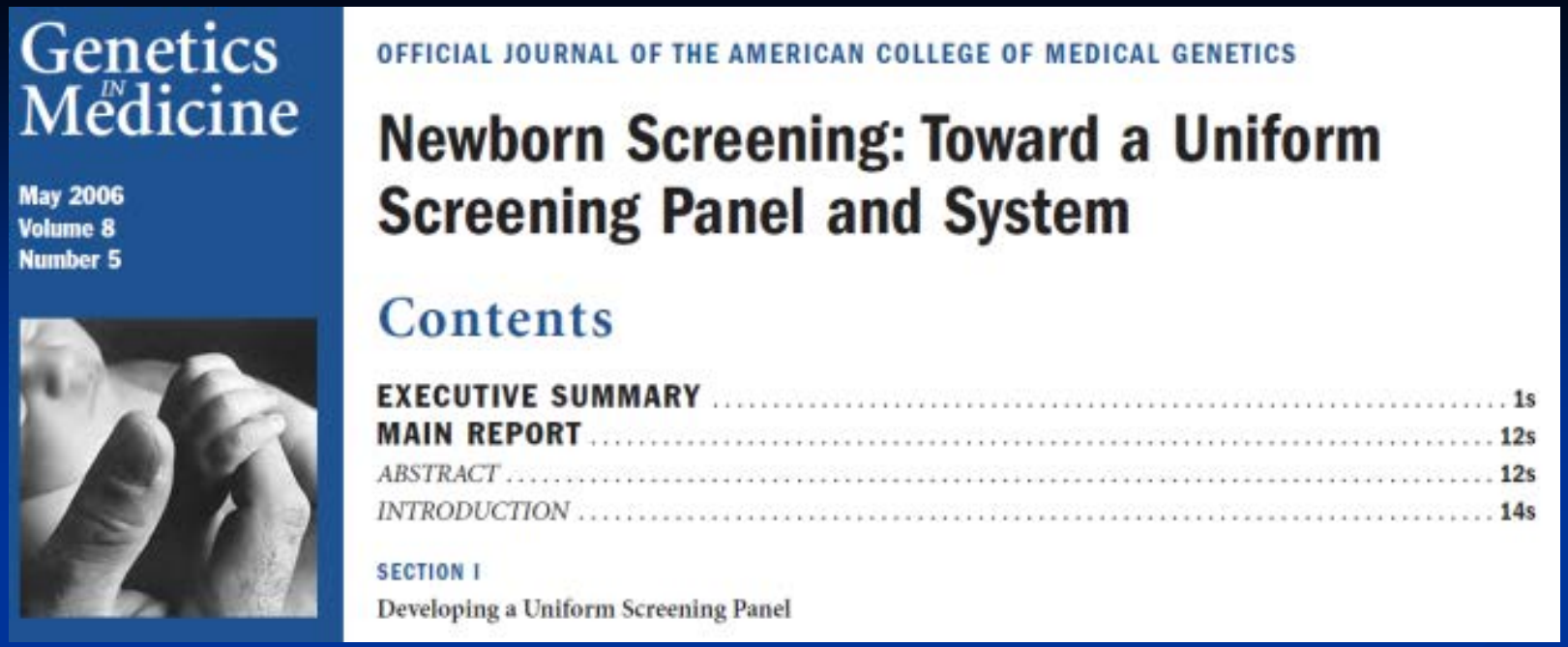
New Jersey NBS Laboratory

SACHDNC

May 11, 2015

Newborn Screening System



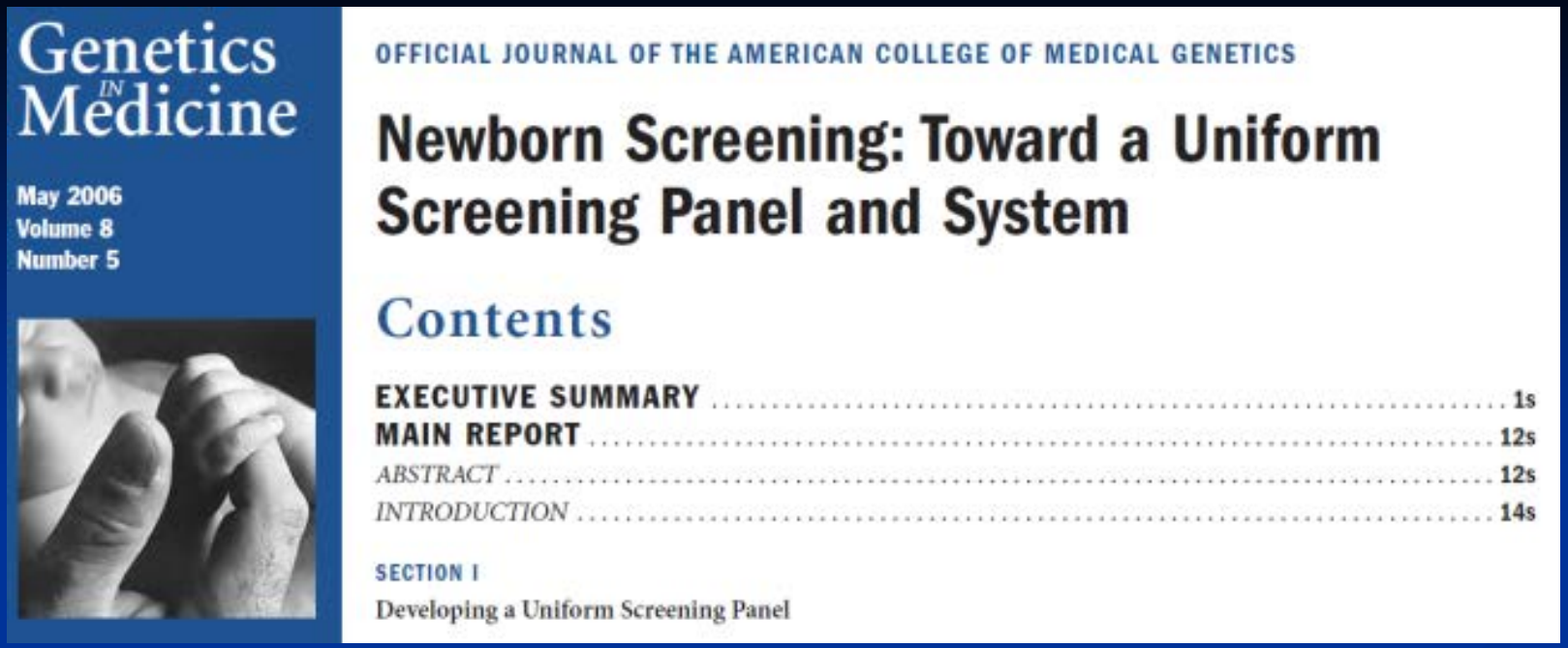


Key Components of Newborn Screening

Education (throughout the process)
Screening, including specimen collection and testing
Follow-up and result reporting
Diagnostic confirmation
Management
Program evaluation and Continuous Quality Improvement

NJ Health
New Jersey Department of Health

State of New Jersey
NEWBORN SCREENING



Total quality management should be applied to newborn screening programs.

As with any programmatic effort, improvements result from careful and continuous monitoring of key steps in the process, the assessment of that information, and the introduction of changes that continuously improve program performance. Uniform and consistent monitoring of system quality indicators can provide information about the relative performance of screening programs.

NJ Health
New Jersey Department of Health

State of New Jersey
NEWBORN SCREENING

- **Quality Assurance (QA)** – all the planned and systematic activities implemented within the quality system, and demonstrated as needed, to provide adequate confidence that an entity will fulfill requirements for quality. **NOTE**: Quality assurance may be said to comprise internal quality assurance and external quality assurance and is interrelated with quality control.

- **Quality Control (QC)** – the operational techniques and activities that are used to fulfill requirements for quality.

- **Quality Indicators (QI)** - a metric that gives an indication of process or output quality and can be used to make comparisons across different Programs

Ensuring Quality

Newborn Screening Quality Assurance Program

QUALITY CONTROL **MIDYEAR REPORT**

Volume 23, No. 1 June 2012

INTRODUCTION

The Newborn Screening Quality Assurance Program (NSQAP), Centers for Disease Control and Prevention (CDC), distributed dried-blood-spot (DBS) quality control (QC) materials for thyroxine (T4), thyroid-stimulating hormone (TSH), 17 α-hydroxyprogesterone (17-OHP), total galactose (TGal), immunoreactive trypsinogen (IRT), phenylalanine (Phe), leucine (Leu), methionine (Met), tyrosine (Tyr), valine (Val), citrulline (Cit), arginine (Arg), succinylacetone (SUAC), and sixteen acylcarnitines (C0, C2, C3, C3DC, C4, C5, C5DC, C5OH, C6, C8, C10, C12, C14, C16, C16OH, C18) to laboratories operating newborn screening programs and to manufacturers of screening test products. Included with each semiannual shipment of QC specimens were instructions for downloading and submitting the paperless data report forms.

This midyear report contains a summary of the QC data submitted during the first half of 2012 by state, contract, and private laboratories in the United States; international participants; and manufacturers of screening test products.

QUALITY CONTROL MATERIALS

The QC specimen lots were provided as 6-month supplies of DBSs on filter paper. DBS QC lots were prepared from whole blood of 50% hematocrit. The QC materials were enriched with predetermined quantities of the selected analytes and dispensed in 100 µL aliquots on GE Healthcare Bio-Sciences Corporation (formerly Whatman Inc.), Westborough, MA, Grade 903; and PerkinElmer Health Sciences (formerly Ahlstrom Filtration LLC), Greenville, SC, Grade 226 filter papers.

A QC shipment for T4, TSH, or 17-OHP consisted of blood-spot materials from three lots per analyte, with each lot containing a different concentration of analyte. A QC shipment for IRT, TGal, Phe, Leu, Met, Tyr, Val, Cit, Arg, SUAC and the acylcarnitines consisted of blood-spot cards from four different lots.

The QC materials were supplied for use as external controls in quantities sufficient to maintain continuity and transcend changes in production lots of routinely used method- or kit-control materials. The external QC materials were intended to supplement the participants' method- or kit-control materials at periodic intervals and to allow participants to monitor the long-term stability of their assays. The QC materials should not be used as routine daily QCs.

PARTICIPANTS' RESULTS

For this midyear report, we compiled the data that each participant reported from five analytic runs of specimens from each QC lot and calculated mean values and standard deviations from these data. Data values outside the 99% confidence interval for each QC lot were not included in the computations. We could not include qualitative data, data submitted as inequalities or ranges, data submitted in unidentified units, or data from more than five analytic runs per specimen lot per participant. Some participants submitted results in units other than those requested on the data-report forms. To ensure that all results are appropriately entered in the CDC database, participants

---- QC DATA ----
see pages 3-33

CDC/APHL

This program is cosponsored by the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL).

Direct inquiries to:
Centers for Disease Control and Prevention (CDC)
4770 Buford Highway, NE, MS/F43
Atlanta, GA 30341-3724

Phone: 770-488-4782
FAX: 770-488-4255
E-mail: NMeredith@cdc.gov

Editor: Nancy Meredith
Production: Sarah Brown
Connie Singleton

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

NewSTEPs

Clinical Laboratory Improvement Amendments

COLLEGE OF AMERICAN PATHOLOGISTS

NJ Health New Jersey Department of Health

State of New Jersey NEWBORN SCREENING

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 61 / No. 2
April 6, 2012

Good Laboratory Practices for Biochemical Genetic Testing and Newborn Screening for Inherited Metabolic Disorders

Prepared by
Bin Chen, PhD[1]
Joanne Mei, PhD[2]
Lisa Kalman, PhD[1]
Shahram Shahangian, PhD[1]
Irene Williams, MMSc[1]
MariBeth Gagnon, MS[1]
Diane Bosse, MS[1]
Angela Ragin, PhD[1]
Carla Cuthbert, PhD[2]
Barbara Zehnbauer, PhD[1]

[1]*Division of Laboratory Science and Standards; Laboratory Science, Policy, and Practice Program Office; Office of Surveillance, Epidemiology, and Laboratory Services*
[2]*Division of Laboratory Sciences; National Center for Environmental Health/Agency for Toxic Substances and Disease Registry*

NJ Health New Jersey Department of Health

State of New Jersey NEWBORN SCREENING

Preanalytic

- Test selection and ordering
- Specimen collection, handling, and delivery
- Specimen receipt and accessioning

Analytic

- Specimen preparation
- Test performance
- Monitoring and verification of test accuracy and results
- Documenting test findings

Postanalytic

- Reporting test results
- Turn around time
- Verifying electronic data transfers
- Records and specimen retention

Establishing a New Test

- Verify manufacturer's
  - Accuracy
  - Precision
  - Reportable range
  - Reference intervals

- Establish assay's
  - Accuracy
  - Precision
  - Analytical sensitvity
  - Analytical specificity
  - Reportable range
  - Reference intervals
  - Other performance characteristics

NJ Health New Jersey Department of Health

State of New Jersey NEWBORN SCREENING

BABY'S LAST NAME *(PRINT)*

SN 13100001

DO NOT WRITE IN THIS AREA!

Birth Date	Date of Sample	Type of Feeding	Antibiotic?	BABY'S MEDICAL RECORD NO.
		☐ Breast ☐ HAL/TPN ☐ Bottle ☐ Other_____	☐ Yes ☐ No	
Birth Time ☐ am ☐ pm	**Sample Time** ☐ am ☐ pm	**Multiple Birth?** ☐ Yes ☐ No If Yes, A, B, C, etc.: _____	**Meconium Ileus?** ☐ Yes ☐ No	**Remarks**
Gender ☐ M ☐ F	**Birthweight** gms	**Transfusion PRIOR to sample collection?** If Yes, give **date and time**: ☐ No ☐ Yes-:	**Gestational Age** wks	

MOTHER'S NAME (LAST, FIRST) *(PRINT)* | Mother's Age | Mother's Telephone No.

Address Apt. #

City, State, Zip

Mother's Race
1 ☐ White
2 ☐ Black or African American
3 ☐ Asian
4 ☐ American Indian/ Alaskan Native
5 ☐ Native Hawaiian or Other Pacific Islander
8 ☐ Other

Mother's Hispanic Origin ☐ Yes ☐ No

Mother's SSN (Last 4 digits)

Collector's Initials / Date:

HOSPITAL NAME AND ADDRESS

Telephone No._____

BABY'S PHYSICIAN NAME AND ADDRESS

Telephone No._____

IBM-1 AUG 13 SPECIMEN SUBMITTED BY: ☐ Hospital ☐ Baby's Physician H5704

New Jersey Department of Health

***INITIAL* NEWBORN SCREENING REQUEST**

SN 13100001

NJDOH/NBS LAB COPY

SN 13100001

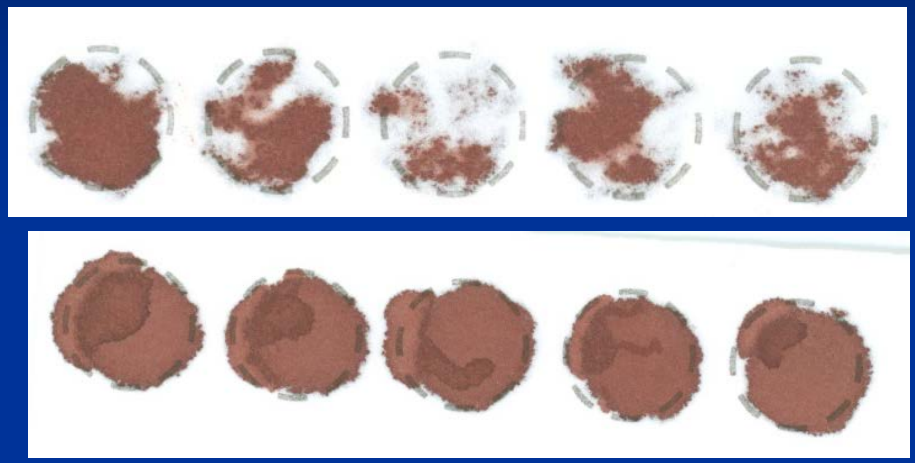
Completely fill 5 circles with blood.

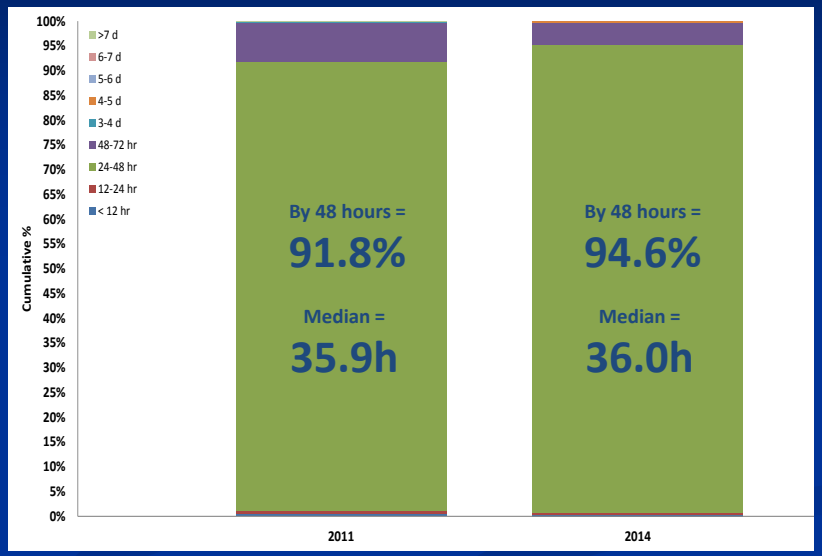
NJ Health New Jersey Department of Health

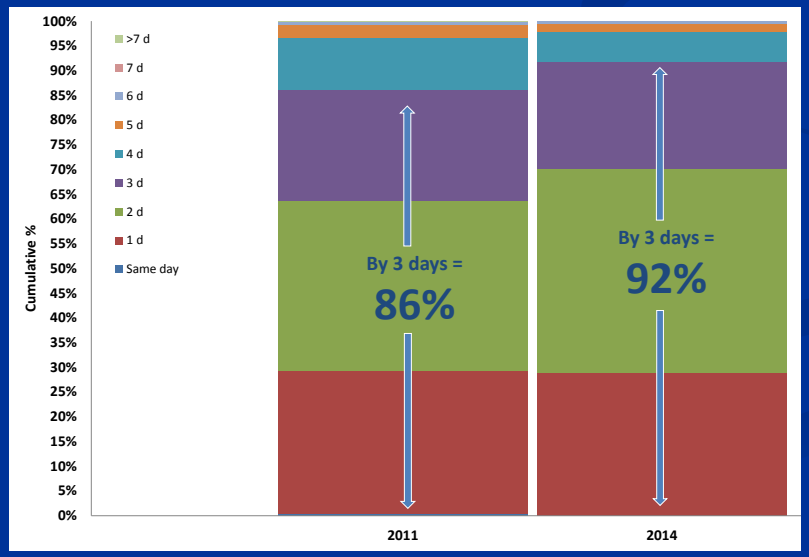
State of New Jersey NEWBORN SCREENING

- CLSI -Clinical and Laboratory Standards Institute www.clsi.org
- LA04-A5 - Blood Collection on Filter Paper for Newborn Screening Programs; Approved Standard - Fifth Edition
- LA04-A5-DVD - Making a Difference Through Newborn Screening: Blood Collection on Filter Paper

Preanalytic Quality

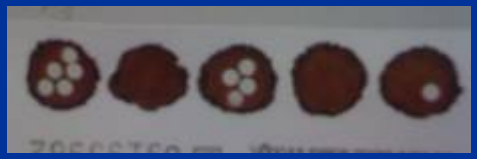







ups
Express Envelope


UNITED STATES
POSTAL SERVICE



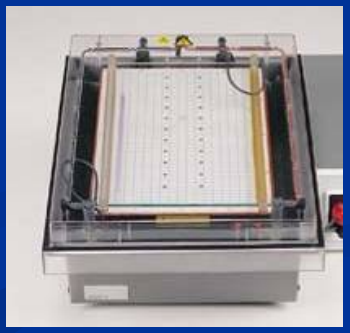
NJ Health
New Jersey Department of Health

State of New Jersey
NEWBORN
SCREENING

Galactosemia
- GALT
- TGAL

Biotinidase Deficiency
- BIO

Amino Acid Disorders
Fatty Acid Disorders
Organic Acid Disorders



Hemoglobinopathies

Cystic Fibrosis
- IRT

Congenital Adrenal Hyperplasia
- 17OHP

Congenital Hypothyroidism
- T4
- TSH

Severe Combined Immunodeficiency

NJ Health
New Jersey Department of Health

State of New Jersey
NEWBORN SCREENING

Rejecting assays is not the purpose of quality control

Process must detect immediate errors caused by test failure

Analytic Quality

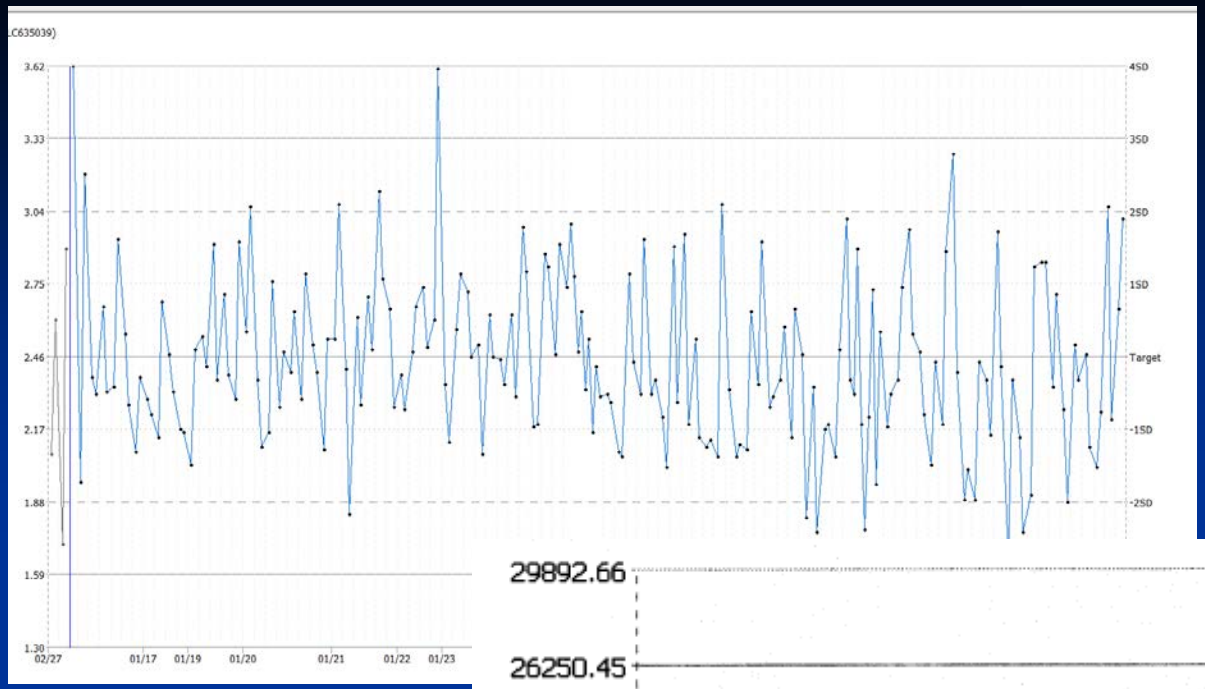
- Material
  - Dried blood spots
    - In-house
    - Commercial vendor
      - Kit
      - Non-kit
      - CDC NSQAP
- Levels
  - Decision points
    - WNL
    - Abnormal
- Establishing laboratory range
  - Replicates ≥ 20 observations
  - Instrument to Instrument
- Frequency
  - ≥ 2 control materials per assay
- Acceptance Criteria
  - Westgard rules
  - Patients
- Monitor
  - Plate
  - Instrument to Instrument
  - Trends
  - Shifts

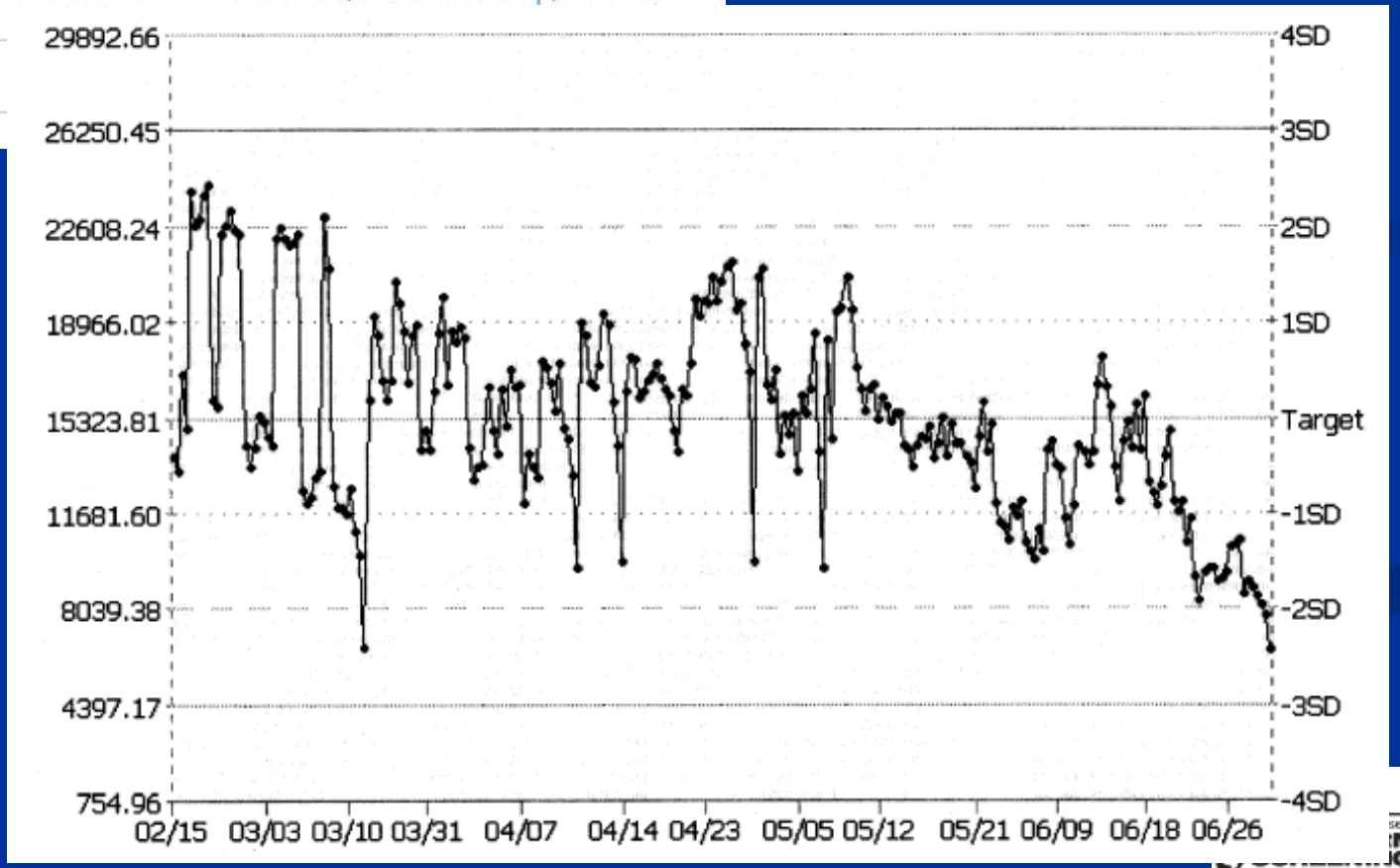
Monitor & Corrective Action

Sample	2015035P1-LOW1	2015035P1-LOW2	Range	2015035P1-HIGH1	2015035P1-HIGH2	Range
C0	139.46	157.12	(123.52 - 181.60)	358.85	342.54	(302.32 - 424.90)
C2	32.49	35.83	(29.79 - 42.99)	73.68	73.62	(61.97 - 90.35)
C3	8.33	9.44	(7.46 - 11.60)	23.56	22.56	(19.13 - 29.75)
C4	1.68	2.65	(1.39 - 4.09)	7.73	5.95	(3.57 - 10.23)
C4 MRM	2.31	2.63	(2.21 - 3.35)	6.68	6.27	(5.59 - 8.77)
C5	1.23	1.06	(0.50 - 1.58)	2.29	2.26	(1.35 - 3.93)
C5 MRM	0.94	1.05	(0.87 - 1.23)	2.49	2.55	(2.06 - 3.44)
C5DC	0.63	0.67	(0.48 - 0.72)	1.53	1.48	(1.24 - 1.90)
C6	0.42	0.63	(0.17 - 1.07)	2.19	1.46	(0.50 - 2.84)
C8	0.8	0.62	(0.24 - 1.08)	1.79	1.4	(0.71 - 2.99)
C10	0.55	0.49	(0.14 - 0.86)	1.28	0.61	(0.40 - 2.26)
C12	2.11	1.9	(1.08 - 2.82)	4.1	5.22	(2.98 - 7.42)
C14	1.99	2.19	(1.06 - 2.62)	3.65	5.43	(2.92 - 6.58)
C16	10.86	10.86	(8.09 - 17.09)	24.34	27.81	(20.27 - 40.85)
C16 MRM	11.7	13.62	(10.62 - 14.70)	31.59	29.63	(25.54 - 37.42)
C18	2.26	2.35	(1.59 - 3.33)	5.2	5.98	(2.66 - 7.40)
C18 MRM	2.36	2.56	(2.02 - 2.98)	4.87	4.67	(4.06 - 5.98)
CIT	161.82	174.12	(128.98 - 191.02)	526.25	509.94	(416.21 - 629.45)
LEU	379.78	575.87	(363.63 - 613.17)	1614.49	1485.48	(1010.70 - 1953.48)
MET	94.2	109.52	(54.32 - 112.76)	321.77	253.68	(191.79 - 392.19)
PHE	192.89	227.81	(167.78 - 254.48)	539.97	656.16	(491.07 - 803.97)
TYR	281.85	391.81	(215.61 - 389.97)	1107.64	999.54	(702.05 - 1294.73)
ARG	6.88	6.33	(3.36 - 7.08)	5.61	5.1	(3.15 - 7.71)

NJ Health
New Jersey Department of Health

State of New Jersey
NEWBORN SCREENING





NJ Health
New Jersey Department of Health

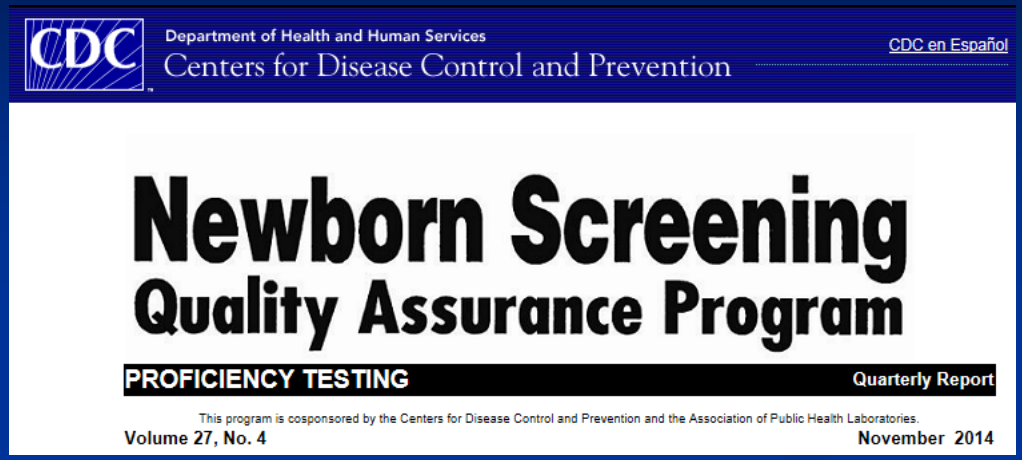
SCID Cutoff Adjustment

>37 weeks	BORD	PRE	Total Abnormal
June 30, 2014 to Oct 7, 2014 26,835 specimens	89 (0.33%)	14 (0.05%)	103 (0.38%)
Oct 8, 2014 to Jan 31, 2015 32,082 specimens	13 (0.04%)	3 (0.009%)	16 (0.05%)

1 Classic SCID, 1 ADA SCID, 1 Leaky SCID, 5 idiopathic T-cell lymphopenia

Proficiency Testing

- External
- Specimen exchange
- Internal


CDC
Department of Health and Human Services
Centers for Disease Control and Prevention
CDC en Español

Newborn Screening Quality Assurance Program

PROFICIENCY TESTING — Quarterly Report

This program is cosponsored by the Centers for Disease Control and Prevention and the Association of Public Health Laboratories.

Volume 27, No. 4 — November 2014

Preanalytic

- Test selection and ordering
- Specimen collection, handling, and delivery
- Specimen receipt and accessioning

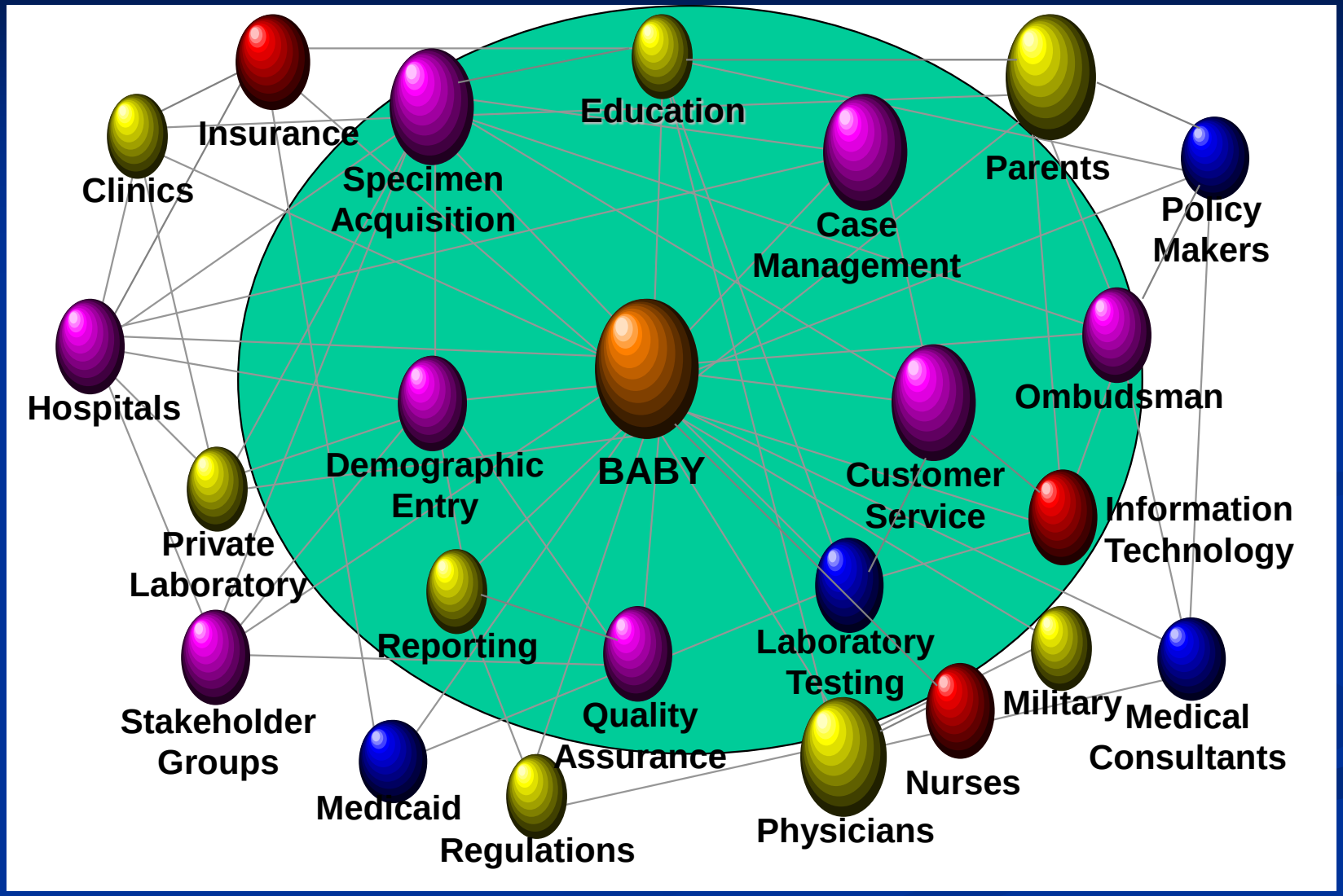
Analytic

- Specimen preparation
- Test performance
- Monitoring and verification of test accuracy and results
- Documenting test findings

Postanalytic

- Reporting test results
- Turn around time
- Verifying electronic data transfers
- Records and specimen retention

Newborn Screening System



Saving Babies for 50 Years
1964 — 2014
State of New Jersey
NEWBORN SCREENING

NJ Health
New Jersey Department of Health

State of New Jersey
NEWBORN SCREENING