OneLab™

A Unified Response to Training Needs

Newborn Screening: System Frameworks and Quality Assurance

July 25, 2024

Agenda

- Introduction
  - *New and relevant OneLab™ Resources*
  - *Today's Presenter*
- *Newborn Screening: System Frameworks and Quality Assurance*
- Q&A
- Upcoming Events

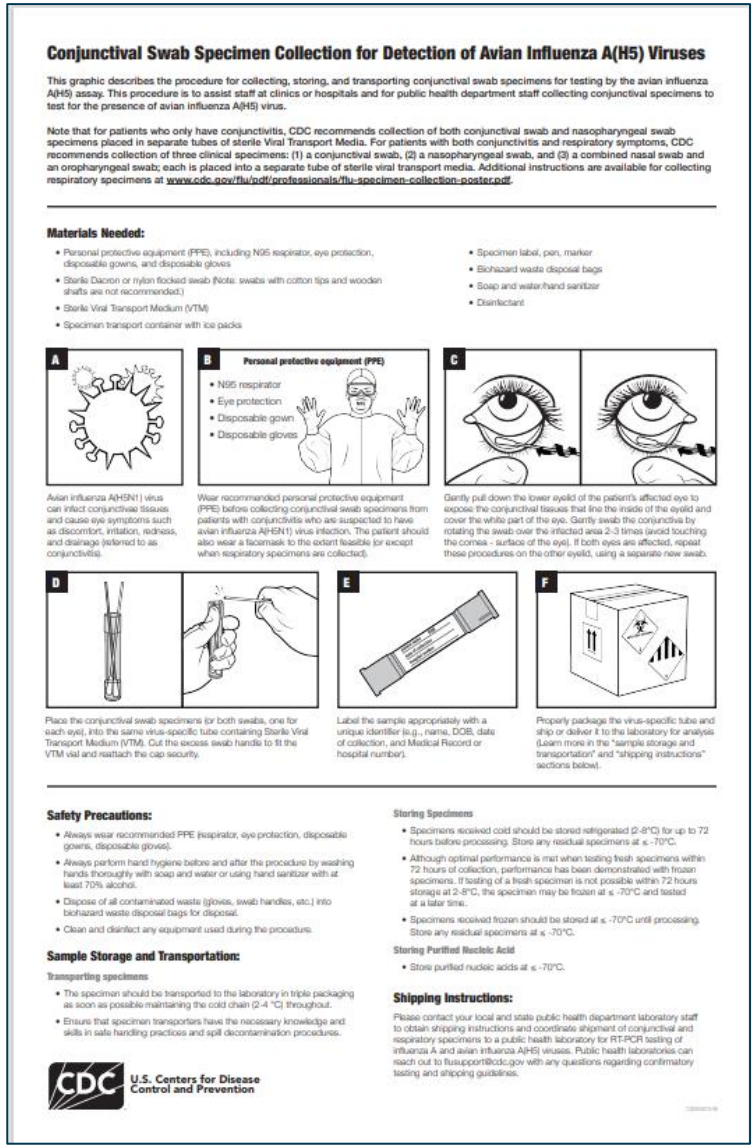
Participant Rules of Engagement for the Webinar Chat

Please keep the following in mind when using the chat feature:

- **Connect with others!** React to what you're hearing, share experiences, and ask questions of your fellow participants!
- **Have a question for the presenter?** Use the Q&A function, *not* the chat.
- **Show Respect and Professionalism.** Inappropriate language, improper conduct, or any form of discrimination may result in removal from the webinar.
- **Remain on Topic.** Ensure your comments are relevant to the topic.
- **Comply with Moderators' Guidance.** If a moderator gives direction regarding chat behavior, please comply accordingly.
- **Report Issues.** Notify moderators if you experience technical difficulties or observe any disruptive behavior.

Avian Influenza A(H5) Virus Desk Reference Graphic

Desk Reference Graphic: Conjunctival Swab Specimen Collection for Detection of Avian Influenza A(H5) Viruses



Conjunctival Swab Specimen Collection for Detection of Avian Influenza A(H5) Viruses

This graphic describes the procedure for collecting, storing, and transporting conjunctival swab specimens for testing by the avian influenza A(H5) assay. This procedure is to assist staff at clinics or hospitals and for public health department staff collecting conjunctival specimens to test for the presence of avian influenza A(H5) virus.

Note that for patients who only have conjunctivitis, CDC recommends collection of both conjunctival swab and nasopharyngeal swab specimens placed in separate tubes of sterile Viral Transport Media. For patients with both conjunctivitis and respiratory symptoms, CDC recommends collection of three clinical specimens: (1) a conjunctival swab, (2) a nasopharyngeal swab, and (3) a combined nasal swab and an oropharyngeal swab; each is placed into a separate tube of sterile viral transport media. Additional instructions are available for collecting respiratory specimens at www.cdc.gov/flu/pdf/professionals/flu-specimen-collection-poster.pdf.

Materials Needed:

- Personal protective equipment (PPE), including N95 respirator, eye protection, disposable gowns, and disposable gloves
- Sterile Dacron or nylon flocked swab (Note: swabs with cotton tips and wooden shafts are not recommended.)
- Sterile Viral Transport Medium (VTM)
- Specimen transport container with ice packs
- Specimen label, pen, marker
- Biohazard waste disposal bags
- Soap and water/hand sanitizer
- Disinfectant

A

Avian influenza A(H5N1) virus can infect conjunctival tissues and cause eye symptoms such as discomfort, irritation, redness, and drainage (referred to as conjunctivitis).

B Personal protective equipment (PPE)

- N95 respirator
- Eye protection
- Disposable gown
- Disposable gloves

Wear recommended personal protective equipment (PPE) before collecting conjunctival swab specimens from patients with conjunctivitis who are suspected to have avian influenza A(H5N1) virus infection. The patient should also wear a facemask to the extent feasible (or except when respiratory specimens are collected).

C

Gently pull down the lower eyelid of the patient's affected eye to expose the conjunctival tissues that line the inside of the eyelid and cover the white part of the eye. Gently swab the conjunctiva by rotating the swab over the infected area 2-3 times (avoid touching the cornea - surface of the eye). If both eyes are affected, repeat these procedures on the other eyelid, using a separate new swab.

D

Place the conjunctival swab specimens (or both swabs, one for each eye), into the same virus-specific tube containing Sterile Viral Transport Medium (VTM). Cut the excess swab handle to fit the VTM vial and reattach the cap securely.

E

Label the sample appropriately with a unique identifier (e.g., name, DOB, date of collection, and Medical Record or hospital number).

F

Properly package the virus-specific tube and ship or deliver it to the laboratory for analysis (Learn more in the "sample storage and transportation" and "shipping instructions" sections below).

Safety Precautions:

- Always wear recommended PPE (respirator, eye protection, disposable gowns, disposable gloves).
- Always perform hand hygiene before and after the procedure by washing hands thoroughly with soap and water or using hand sanitizer with at least 70% alcohol.
- Dispose of all contaminated waste (gloves, swab handles, etc.) into biohazard waste disposal bags for disposal.
- Clean and disinfect any equipment used during the procedure.

Sample Storage and Transportation:

Transporting specimens

- The specimen should be transported to the laboratory in triple packaging as soon as possible maintaining the cold chain (2-4 °C) throughout.
- Ensure that specimen transporters have the necessary knowledge and skills in safe handling practices and spill decontamination procedures.

Storing Specimens

- Specimens received cold should be stored refrigerated (2-8°C) for up to 72 hours before processing. Store any residual specimens at ≤ -70°C.
- Although optimal performance is met when testing fresh specimens within 72 hours of collection, performance has been demonstrated with frozen specimens. If testing of a fresh specimen is not possible within 72 hours storage at 2-8°C, the specimen may be frozen at ≤ -70°C and tested at a later time.
- Specimens received frozen should be stored at ≤ -70°C until processing. Store any residual specimens at ≤ -70°C.

Storing Purified Nucleic Acid

- Store purified nucleic acids at ≤ -70°C.

Shipping Instructions:

Please contact your local and state public health department laboratory staff to obtain shipping instructions and coordinate shipment of conjunctival and respiratory specimens to a public health laboratory for RT-PCR testing of influenza A and avian influenza A(H5) viruses. Public health laboratories can reach out to flusupport@cdc.gov with any questions regarding confirmatory testing and shipping guidelines.

CDC U.S. Centers for Disease Control and Prevention

OneLab™

New Resource!

Mini Lesson

Disclaimer

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Today's Presenter

Carla Cuthbert, PhD, FACMG

Branch Chief

Newborn Screening and Molecular Biology Branch (NSMBB)

US Centers for Disease Control and Prevention (CDC)

National Center for Environmental Health

The Newborn Screening System and the Role of Quality Assessments and Technical Assistance

Source: Microsoft Powerpoint stock images

Carla Cuthbert, PhD, FACMG
Branch Chief
Newborn Screening and Molecular Biology Branch
Division of Laboratory Sciences
National Center for Environmental Health

Thursday 25th July 2024
ONELAB Network Webinar

Outline

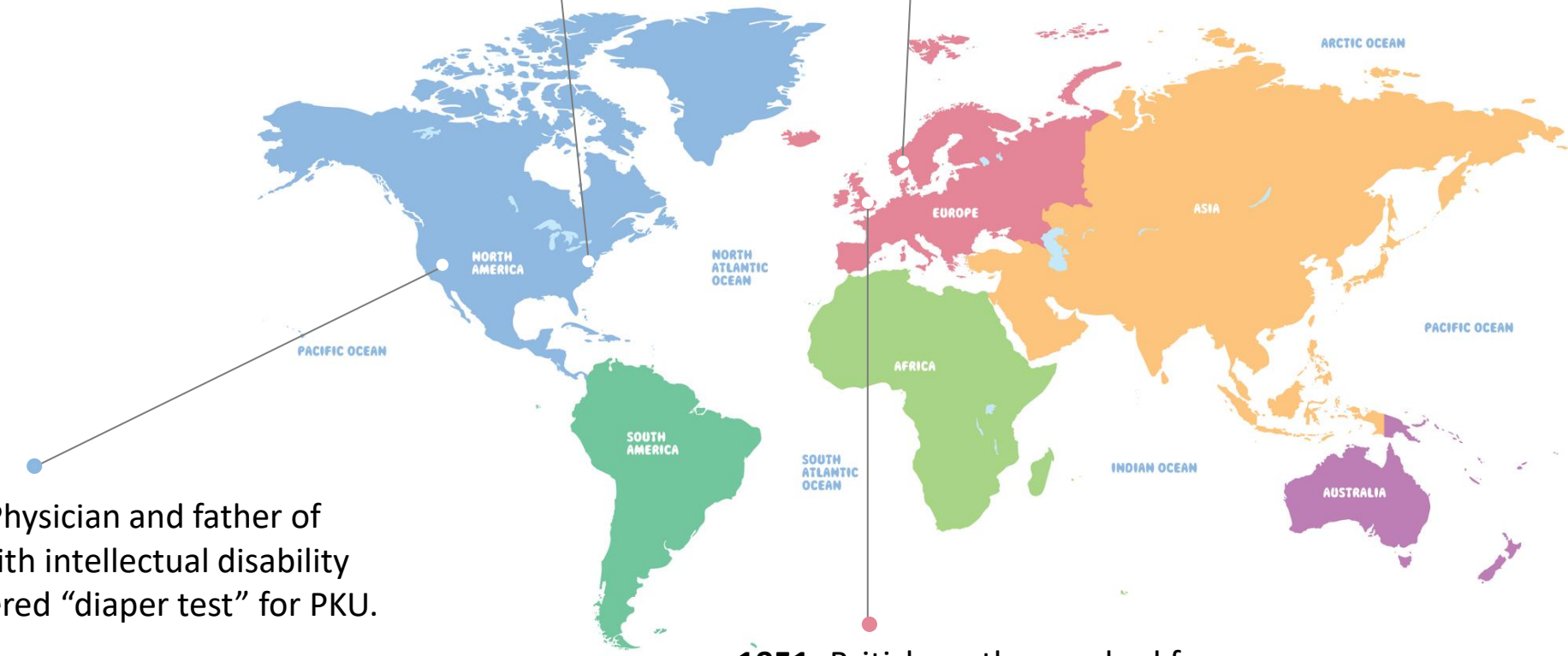
1. History and Evolution of Newborn Screening
2. The Newborn Screening System
3. Importance of Quality Assurance and Technical Assistance Across the System

History and Evolution of Newborn Screening

Newborn Screening: The Role of Advocacy

1958-61: Dr. Robert Guthrie developed and refined the bacterial inhibition assay for detection of PKU at birth.

1934: Norwegian mother relentlessly pushed her physician to understand cause of children's intellectual disability – **led to discovery of PKU.**



1957: Physician and father of child with intellectual disability discovered "diaper test" for PKU.

1951: British mother pushed for treatment for her child with PKU – **led to the creation of phe-free formula.**

Source: Getty stock images, used with permission.

Newborn Screening as a Public Health Program

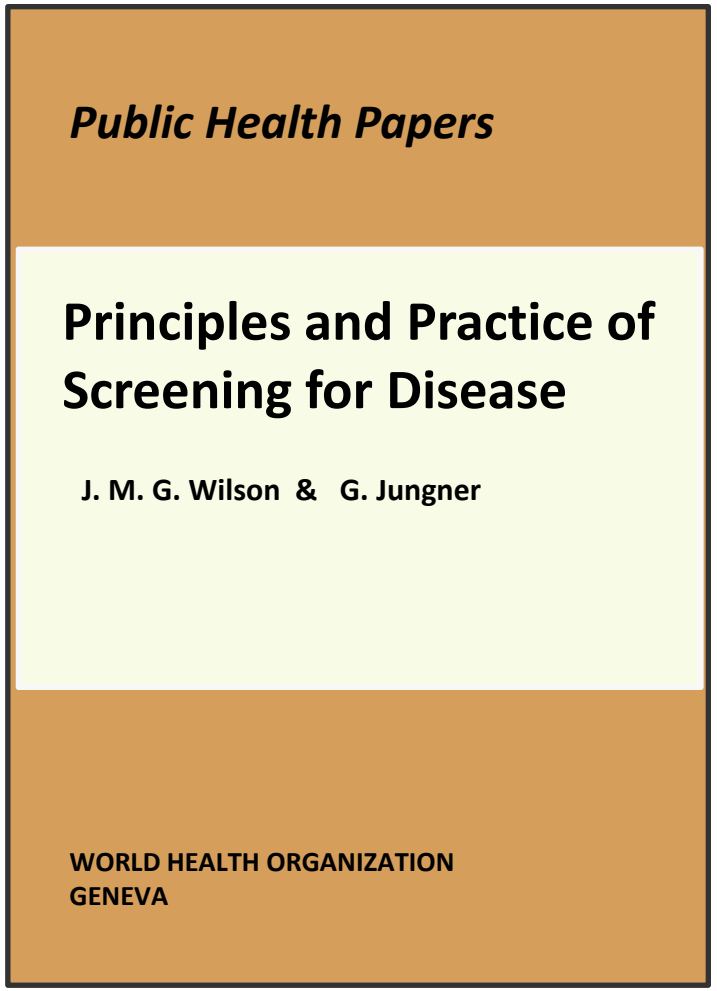
- Dr. Guthrie felt strongly that **all children** should be tested for PKU.

- He worked with public health officials to mandate this screening rather than rely on medical center implementation.

Source: Getty stock images, used with permission.

1969 World Health Organization Report

"The central idea of early disease detection and treatment is essentially simple. However, the path to its successful achievement is far from simple though sometimes it may appear deceptively easy."



Source: Graphic created by CDC-DLS

Image source: Principles and Practice of Screening for Disease. Geneva: World Health Organization; 1968. License CC BY-NC-SA 3.0 IGA
Website Link for PDF of Report: Principles and practice of screening for disease (who.int)

Wilson and Jungner Principles

1. Important health problem
2. Accepted treatment
3. Available centers for diagnosis and treatment
4. Recognizable latent or early symptomatic stage
5. Suitable test or examination
6. Acceptable to the population
7. Natural history should be understood
8. Agreed policy on whom to treat
9. Cost of screening/diagnosis/treatment should be weighed against possible expenditure on medical care
10. Case-finding should be a continuing process and not “once and for all”

Slow and Steady Expansion

- **From 1963 to early 1990s, only 4 more diseases were added**
  - Congenital Hypothyroidism
  - Galactosemia
  - Congenital Adrenal Hyperplasia
  - Sickling Hemoglobinopathies
- **Pace was largely limited by technology and assay availability**
- **“One disease – One assay” paradigm limited the ability to add**

New Technologies Foster Faster Expansion

Tandem Mass Spectrometry and Multiplexing

- Allows for analysis of multiple analytes from one small sample
- New paradigm of “Many diseases – one assay”
  - Unclear how many diseases are truly detectable via MS/MS and which one are included in newborn screening

Nucleic Acid Extraction

- Ability to easily extract DNA allows for molecular-based assays in newborn screening to improve upon sensitivity and specificity

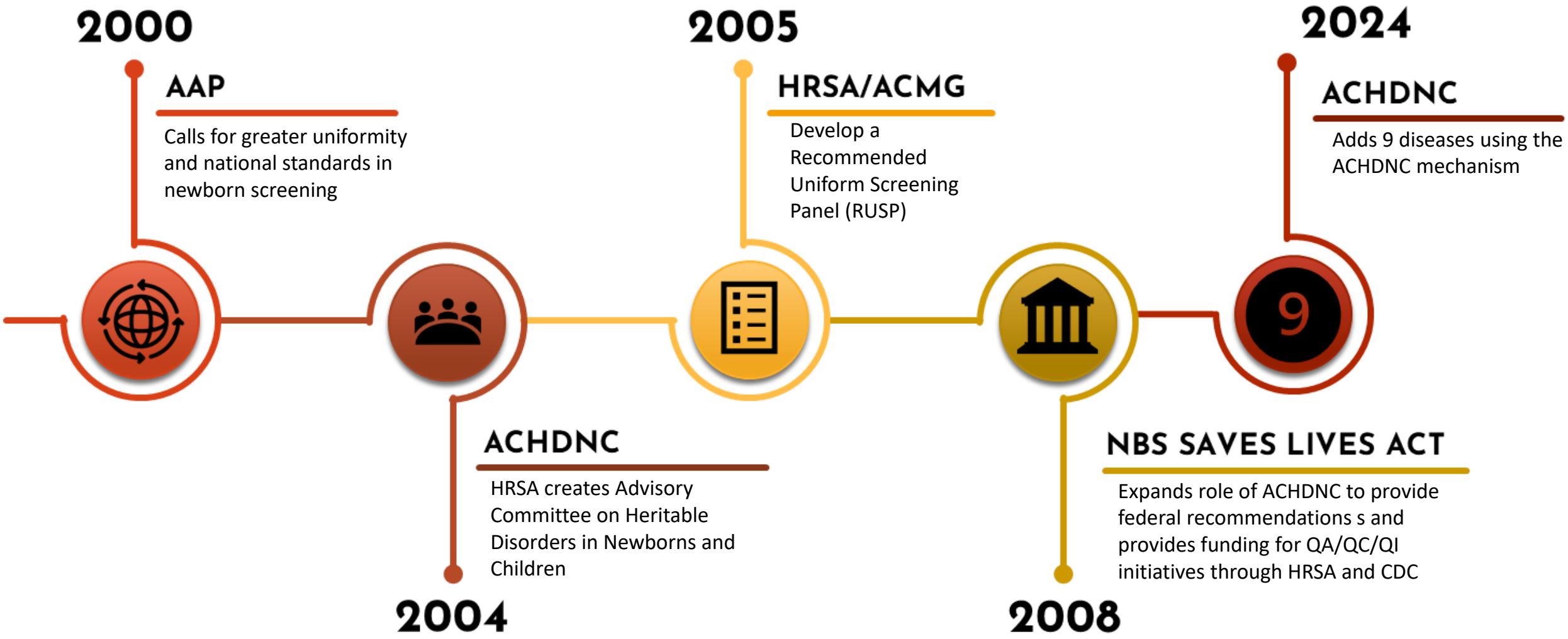
Technology No Longer Primary Limiting Factor…

So the Question Becomes…

Just Because We Can… Should We?

And if We Should… How Do We?

Developing a System of Federal Guidance



Source: Graphic created by CDC-DLS

The Federal Recommended Uniform Screening Panel

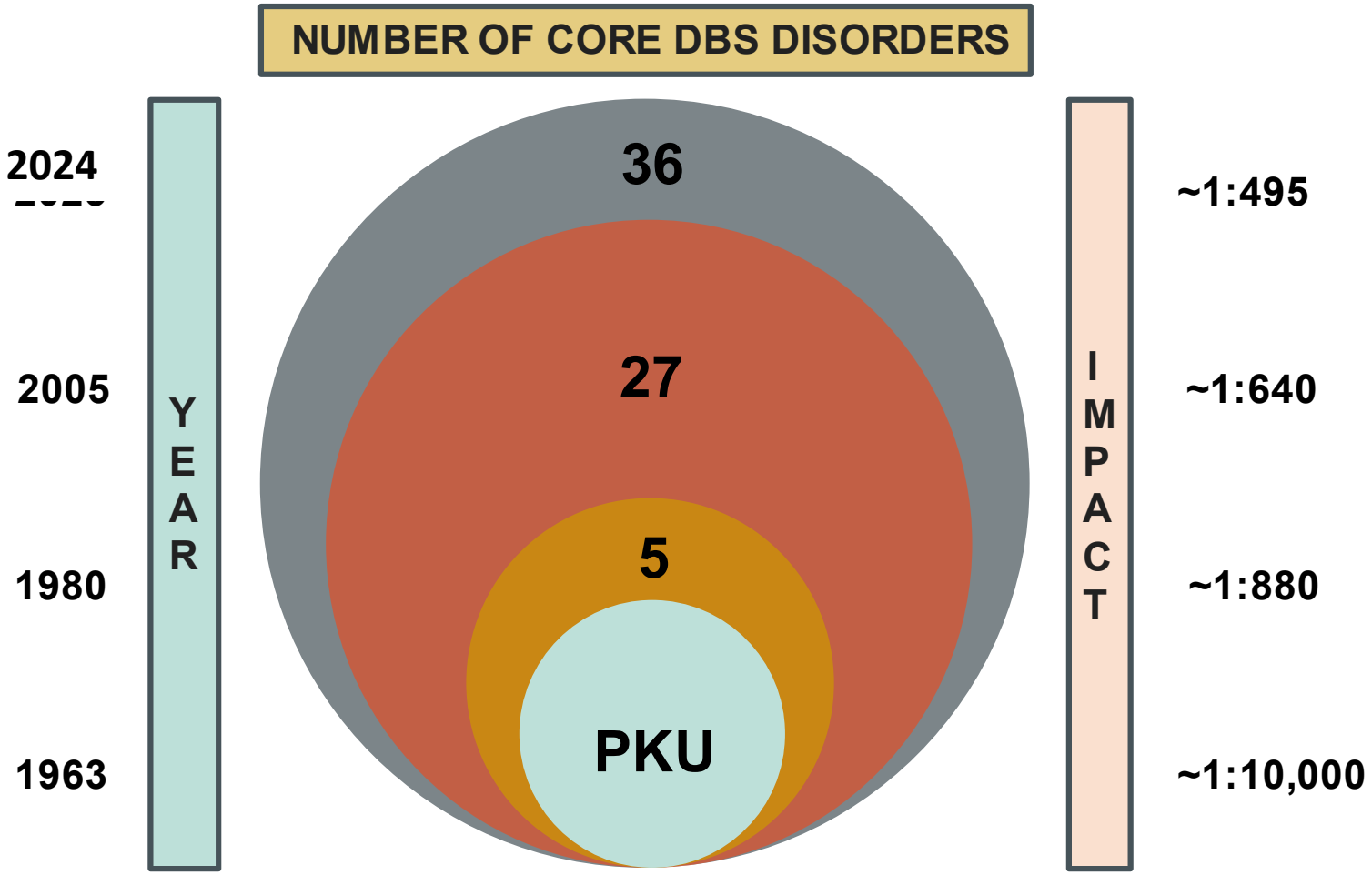
Recommended Uniform Screening Panel:

List of disorders that the Secretary of the Department of Health and Human Services (HHS) recommends for states to screen as part of their state universal newborn screening (NBS) programs.

Core Diseases	Secondary Diseases
Diseases targeted by the assay	Incidentally picked up through screening for core condition
Typically meet all screening criteria	May or may not meet all screening criteria
38 core conditions (36 DBS and 2 point-of-care)	26 secondary conditions

Source: Graphic created by CDC-DLS

Status of Expansion: Expanding the Impact

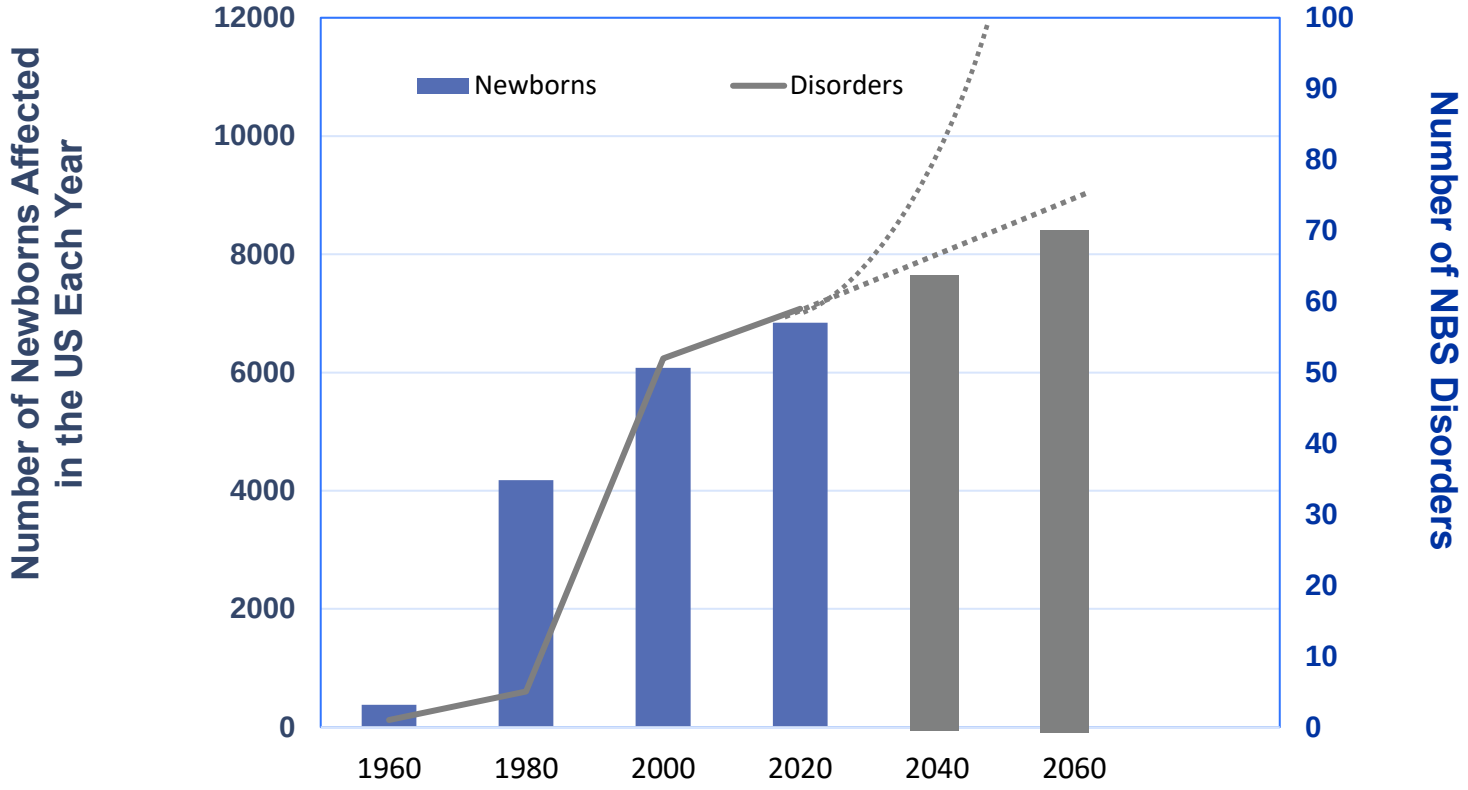


Source: Graphic created by CDC-DLS

Future: Ongoing Expansion

- Expansion of screening to include more and more rare diseases
- More diseases with more complex testing

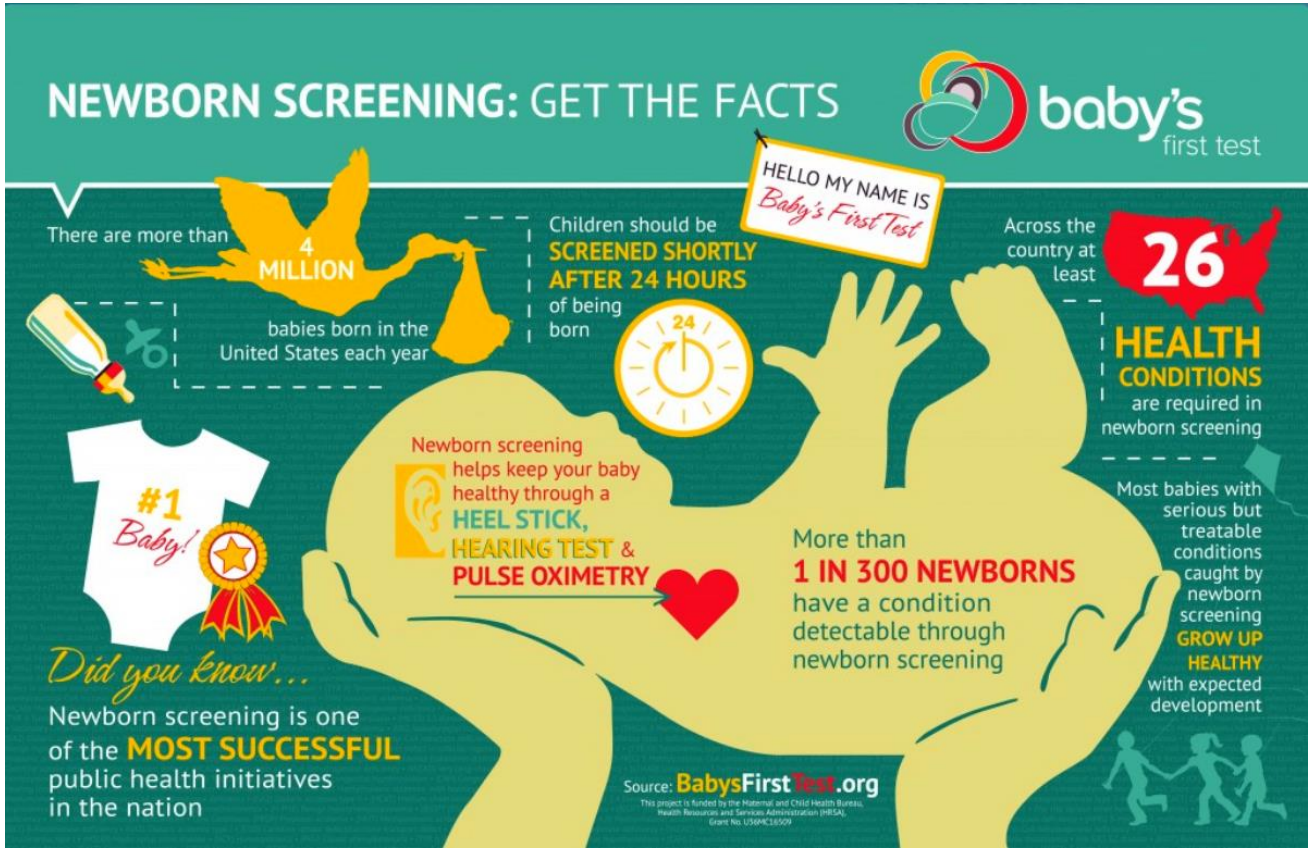
Predicted Increases in Newborn Screening Diseases and Number of Affected Newborns



1) Recommended Uniform Screening Panel (primary and secondary conditions) https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp/index.html .
2) Estimated birth prevalence and from Sontag MK, et al. MMWR 2020;69:1265–1268.

Newborn Screening: A Successful Public Health Program

In 2011, newborn screening was named one of ten great public health achievements of the 20th century.



Infographic source: babysfirsttest.org

The Newborn Screening System

Newborn Screening Premise: Four Key Takeaways

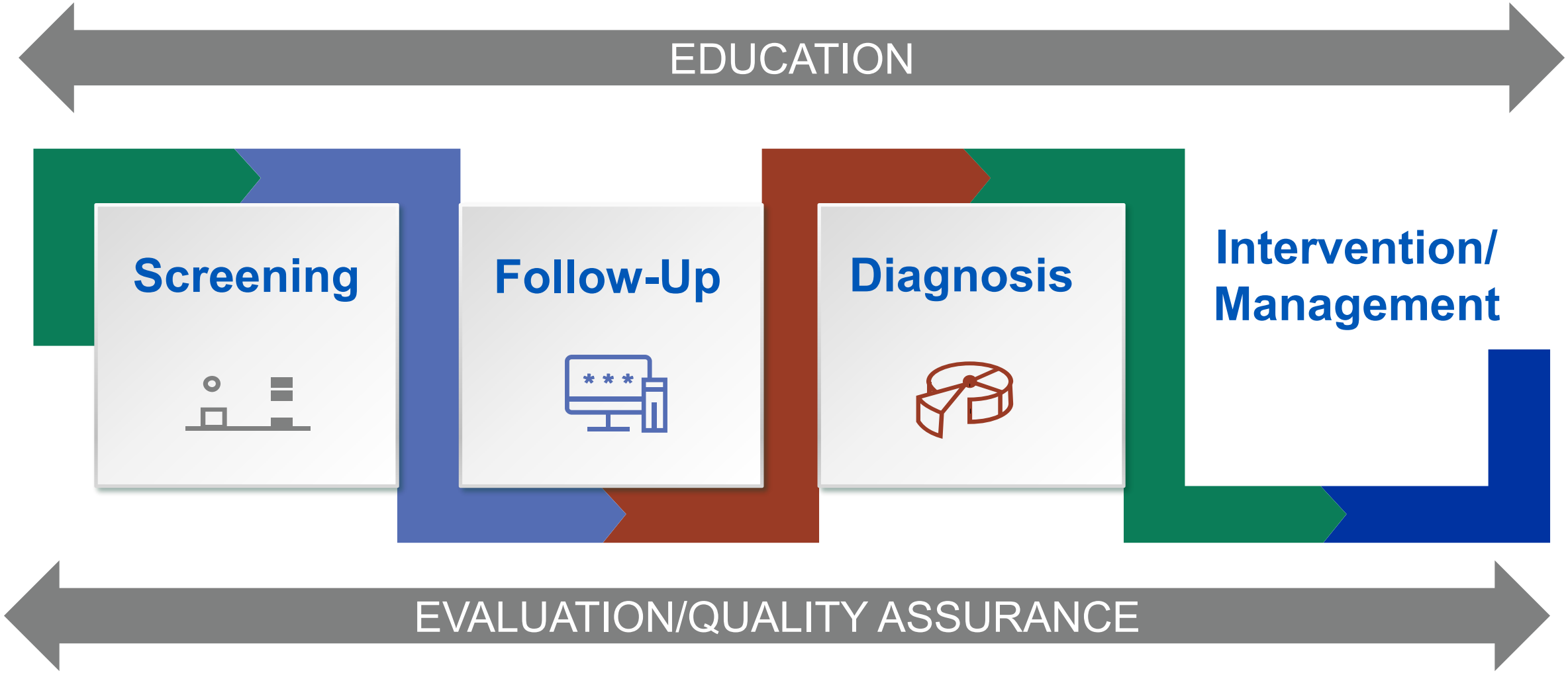
1. Newborn screening programs are **PUBLIC HEALTH** programs
   - Successful programs require knowledge and coordination from multiple partners.

2. Newborn screening programs are **STATE-BASED**
   - Variations between Newborn Screening Programs exist from state-to-state.

3. Newborn screening programs are **OPT-OUT** programs
   - Default is for NBS to occur, but parents may refuse on behalf of their child.

4. Newborn screening programs are designed to detect **TREATABLE** conditions
   - Disorders on the newborn screening panel must meet certain criteria.

Newborn Screening System: Six Parts



Source: Graphic created by CDC-DLS

Legal Foundations of Newborn Screening

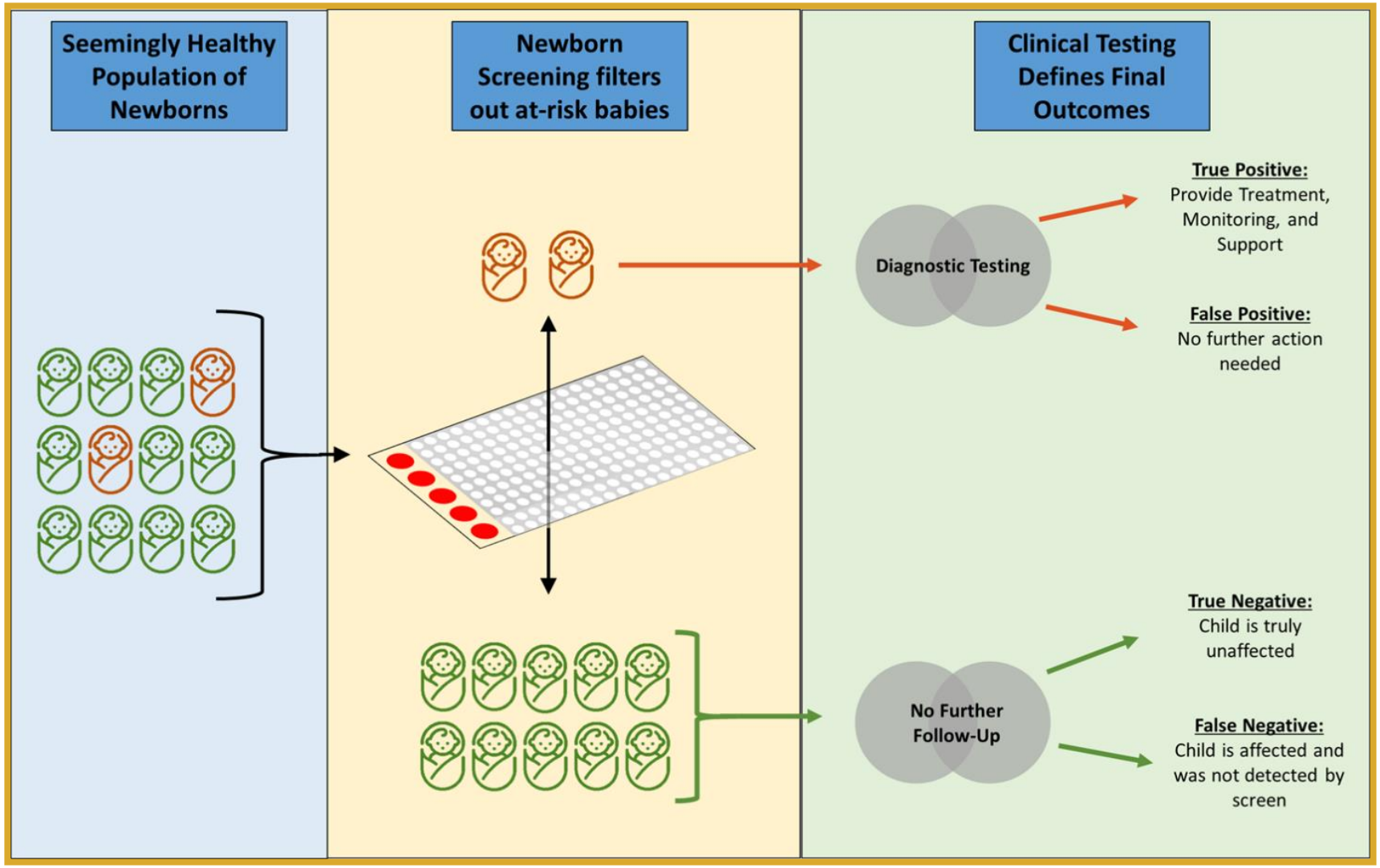
Newborn Screening as a Mandate

- Parents can opt-out…

Legal and Constitutional Foundations of Newborn Screening

- Tenth Amendment
  - States have the power to regulate the receipt of medical care to protect public health
- Common law doctrine of *parens patriae*
  - Permits states to make decisions for the health and well-being of citizens who cannot speak on their own behalf

Newborn Screening as a Risk Assessment



Source: Graphic created by CDC-DLS

The DBS Screening Process: Pre-Analytical

Families should be provided education about screening BEFORE the sample is collected.

Blood spot samples are recommended to be collected between 24 – 48 hours of age.

Specimens are dried horizontally for at least 3 hours prior to submission.

Specimens should be sent to the state screening program and received within 24 hours of collection.

Source: Graphic created by CDC-DLS

The DBS Screening Process: Analytical

Specimens are accessioned and demographic information is entered.

Small punches are taken out of the blood spots and testing is typically done in 96 well plates.

Specimens are analyzed using biochemical and/or molecular techniques.

Results are entered and verified by laboratory staff and communicate to follow-up staff.

Source: Graphic created by CDC-DLS

The DBS Screening Process: Post-Analytical

Results should be available prior to 7 days after birth (actionable results may be available sooner).

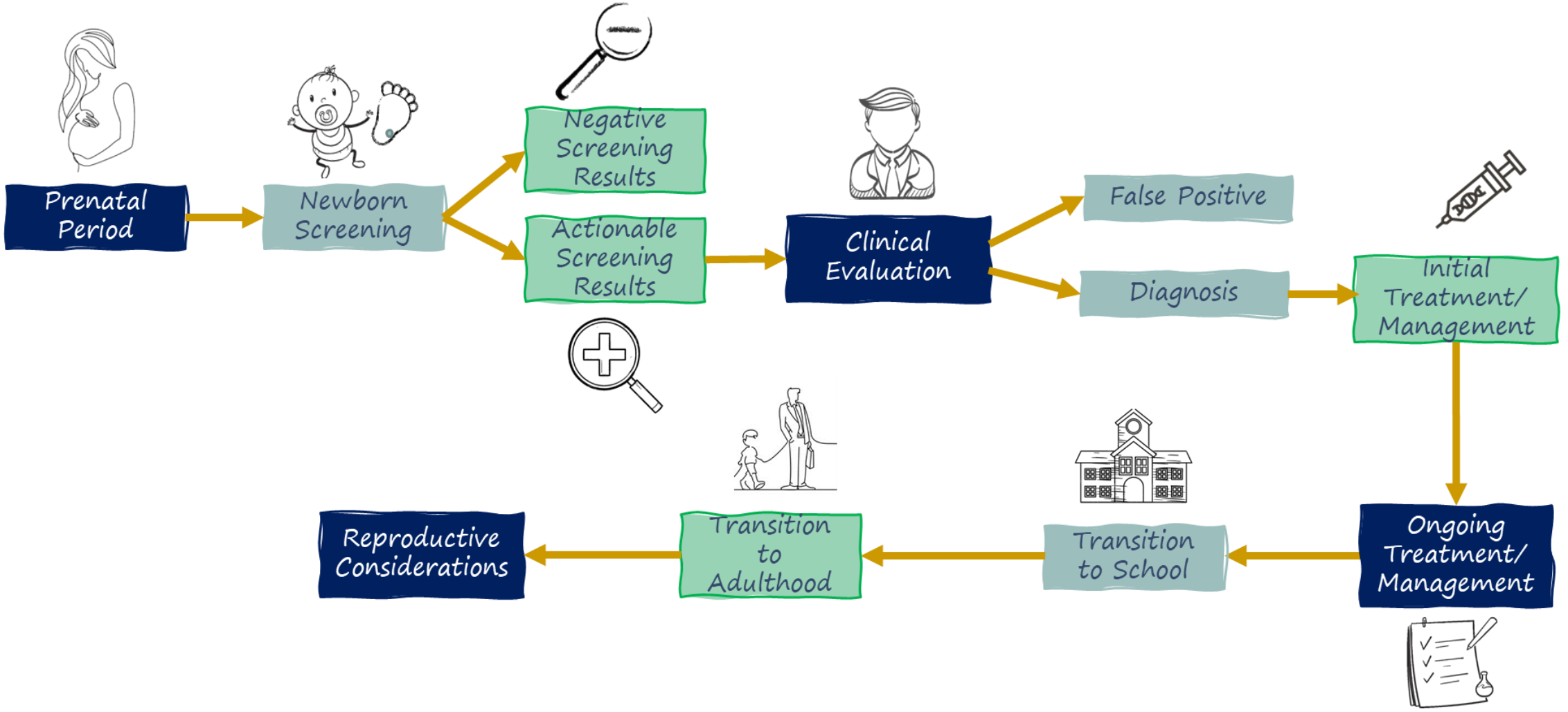
Positive results are called out to the primary care provider and/or specialist.

Normal results are provided to the submitter and should be forwarded to the primary care provider.

Family should be notified by the primary care provider/specialist as soon as possible.

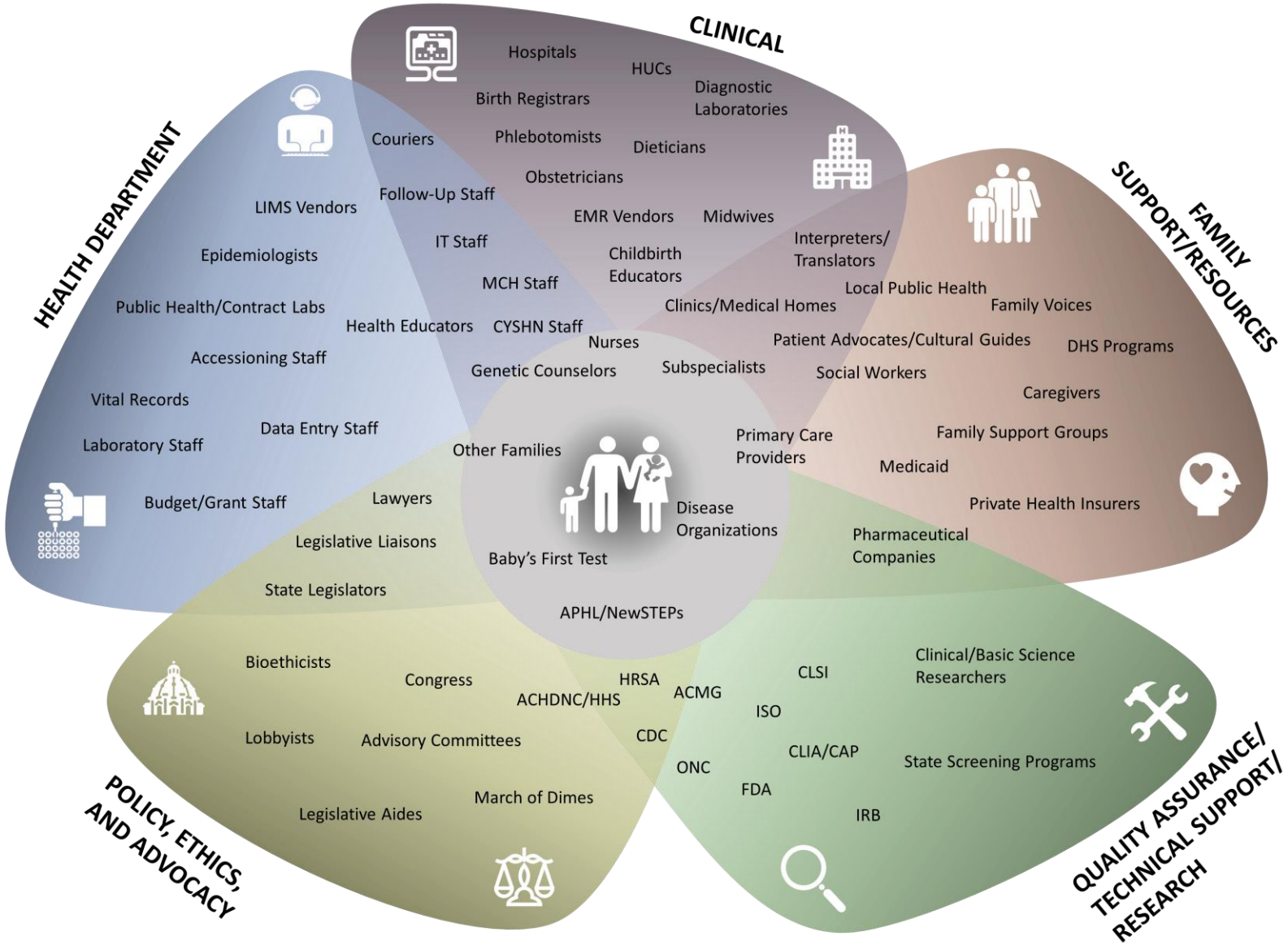
Source: Graphic created by CDC-DLS

The Full Newborn Screening Journey



Source: Graphic created by CDC-DLS

The Newborn Screening System of Partners



Source: Graphic created by CDC-DLS

The Role of Various Agencies and Programs in Supporting Newborn Screening

CAP

- Provides accreditation to laboratories
- Voluntary accreditation signifying a laboratory's commitment to achieving and maintaining excellence in laboratory medicine

CDC

- Oversees NSQAP program for laboratories
- Provides TA and funding to APHL and state NBS programs (lab/data-focused)
- Developing ED3N Data Platform

CMS

- Regulates all clinical laboratory testing on humans through CLIA
- Provides health coverage through Medicaid and CHIP

FDA

- Oversees drug development, laboratory developed testes, AI/ML

HRSA

- Oversees ACHDNC/RUSP
- Provides funding to APHL and state NBS programs (QI/service-focused)

NIH/NICHD

- Provides funding for NBS-related research and pilot studies

Source: Graphic created by CDC-DLS

CAP: College of American Pathologists
CDC: Centers for Disease Control and Prevention
NSQAP: Newborn Screening Quality Assurance Program
TA: Technical Assistance
ED3N: Enhancing Data-driven Disease Detection in Newborns

APHL: Association of Public Health Laboratories
CMS: Centers for Medicare and Medicaid Services
CLIA: Clinical Laboratory Improvement Amendments
CHIP: Children's Health Insurance Program
FDA: Food and Drug Administration

HRSA: Health Resources and Services Administration
ACHDNC: Advisory Committee on Heritable Disorders in Newborns and Children
RUSP: recommended Uniform Screening Panel
NIH: National Institutes of Health
NICHD: National Institute of Chile Health and Human Development

State-Based Nature of Newborn Screening Results in Variations in Practice

- **States vary in all parts of NBS**
  - How Disorders are Added
  - Number of Disorders Screened
  - Testing strategies
  - Follow-up practices
  - Funding structure
  - Infrastructure and Organization
  - Working Hours/Days
  - Storage/Use of DBS

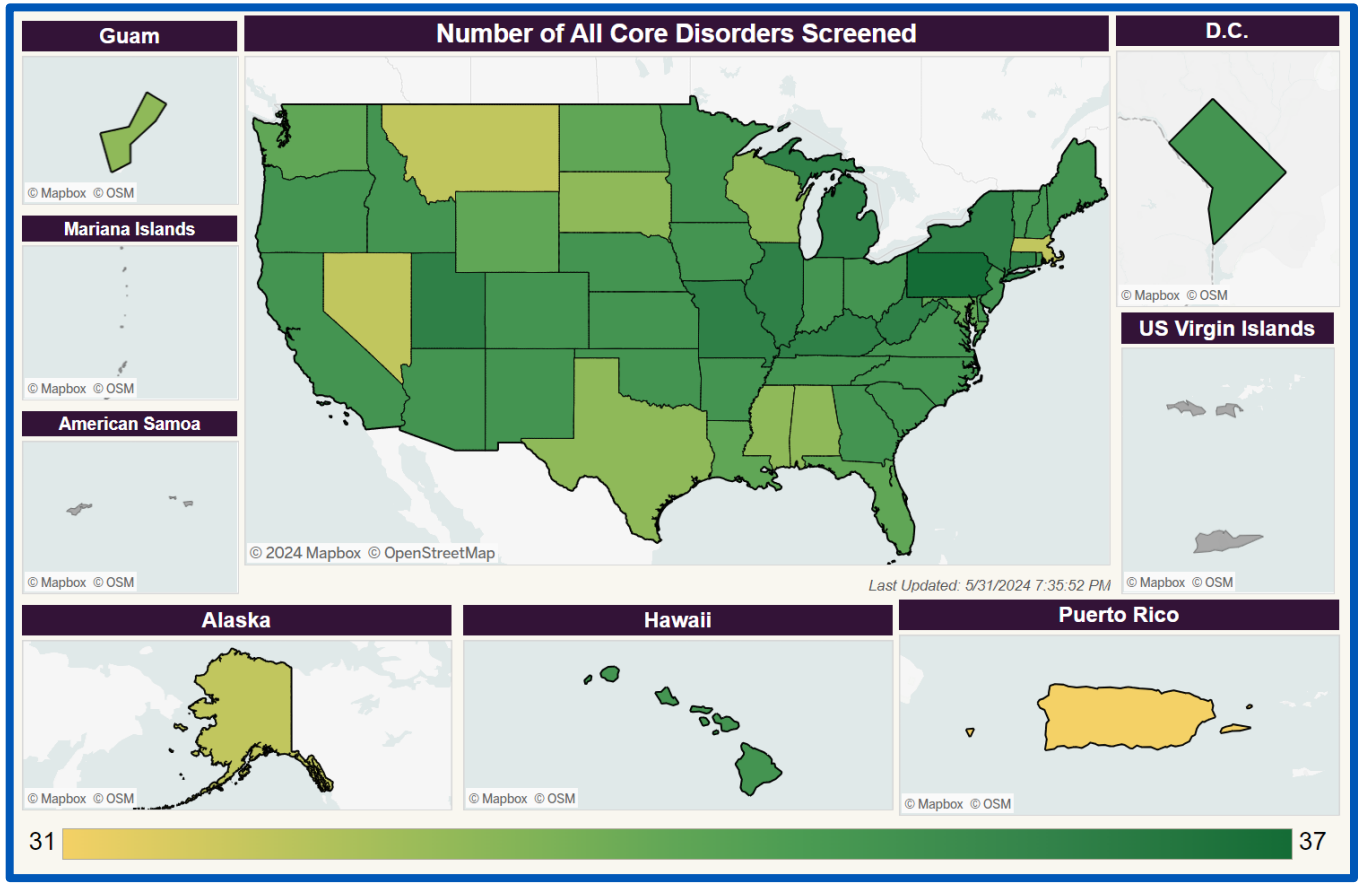


Image Source: https://www.newsteps.org/resources/data-visualizations/newborn-screening-status-all-disorders

Resources

Centers for Disease Control and Prevention

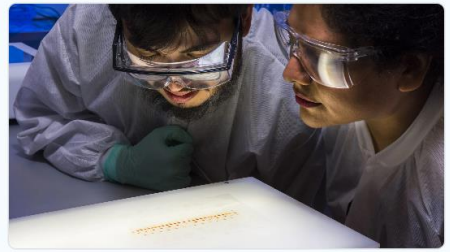
- **Newborn Screening and Molecular Biology Branch**

- **Provides:**
  - Laboratory method design, development, and evaluation
  - Quality improvement of laboratory methods
  - Technical expertise and technology transfer
  - Quality assurance materials
  - Data harmonization
  - Training materials

Supporting State Newborn Screening Laboratories | Newborn Screening | CDC

AT A GLANCE

The Newborn Screening Quality Assurance Program (NSQAP) develops analytical methods to measure substances in dried blood spots (DBSs) and produces certified DBS quality-control and reference materials for newborn screening tests. Because of NSQAP, parents and doctors in the United States and worldwide can trust the results of newborn screening tests.



Access to the NSQAP Participant Portal | Newborn Screening | CDC

For questions reach out to the following mailbox: nsqapdmt@cdc.gov

Clinical and Laboratory Standards Institute (CLSI)

Newborn Screening Guidelines and Standards:

- Covers various aspects of newborn screening, including sample collection, testing methodologies, result interpretation, and follow-up procedures.
- Can be used to ensure high-quality, consistent, and reliable testing processes.

NBS01
Dried Blood Spot Specimen Collection for Newborn Screening

NBS02
Newborn Screening Follow-up and Education

NBS03
Newborn Screening for Preterm, Low Birth Weight, and Sick Newborns

NBS04: MS/MS	NBS08: Hemoglobinopathies	NBS12: Galactosemia
NBS05: Cystic Fibrosis	NBS09: XALD	NBS13: SMA
NBS06: SCID	NBS10: Congenital Hypothyroidism	NBS14: Lysosomal Diseases
NBS07: Pompe	NBS11: Congenital Adrenal Hyperplasia	

Website Source: https://clsi.org/

Newborn Screening Technical assistance and Evaluation Program (NewSTEPs)

Source:
https://www.newsteps.org/

- **NewSTEPs**
  - Overseen by the Association of Public Health Laboratories (APHL)
- **Provides**:
  - Data
  - Technical Assistance
  - Continuous Quality Improvement
  - Training

Importance of Quality Assurance and Technical Assistance Across the System

Quality Assurance in Newborn Screening

Quality assurance (QA) is the monitoring and evaluation of the various aspects of a system to ensure that standards of quality are being met.

Newborn screening QA is a dynamic process of defining and measuring the quality of performance of the ***entire*** screening process.

Internal and external QA activities are needed for continuous quality improvement.

CDC owned image

Quality Assurance: The Key to Better Health Outcomes

GOOD PRACTICE

Understanding of best and promising practices in laboratory t esting and follow-up.

STANDARDS

Using standard practices and policies for both laboratory testing and follow-up. Promoting use of published standards.

MONITORING

Ongoing monitoring and evaluation of pr ocesses and outcomes to identify gaps an d improvement needs.

SITE VISITS

Assessing processes & performance measures, reviewing operating procedures, and assessing needed improvements through external visits.

REPORTS

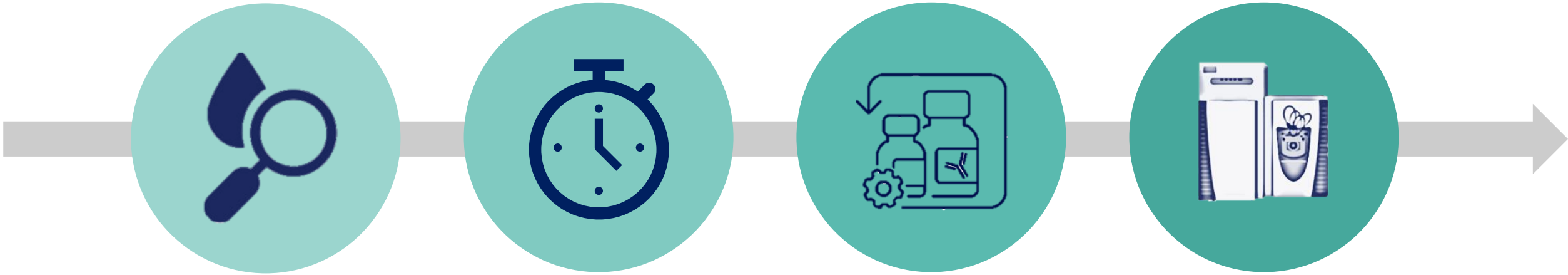
Running routine internal reports and providing external reports t o partners to identify gaps and tr ack progress.

TRAINING

Improving technical capabilities t o enhance processes through continuous education and training for all partners.

Source: Graphic created by CDC-DLS

Quality Assurance in Newborn Screening: Pre-Analytical



Quality of specimens measured against defined criteria

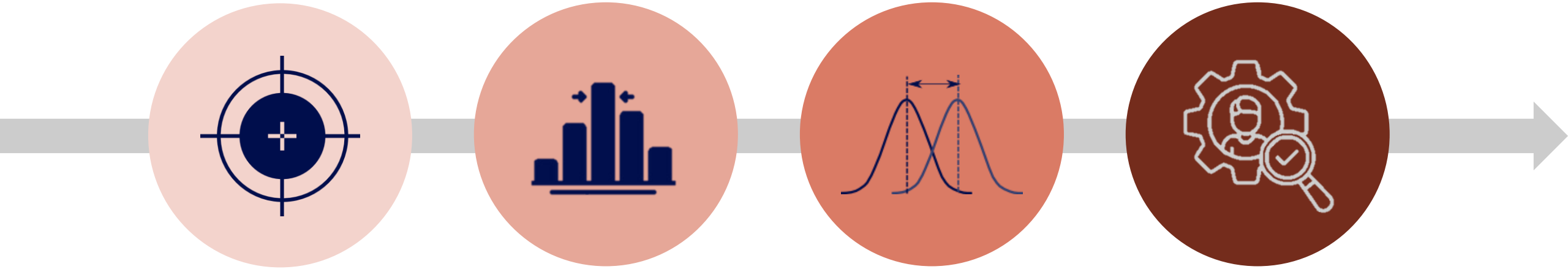
Timing of specimen collection and receipt

Kit and reagent lot

Instrument performance and preventative maintenance

Source: Graphic created by CDC-DLS

Quality Assurance in Newborn Screening: Analytical



Monitoring results from calibrators, standards, and controls

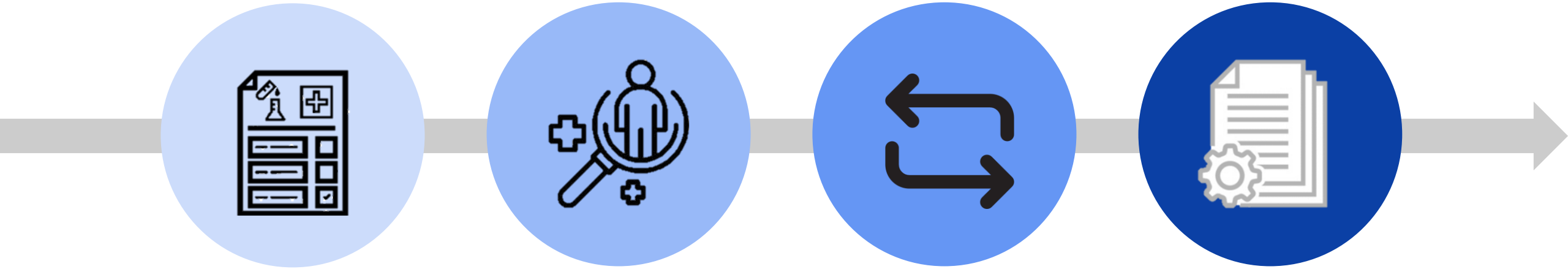
Monitoring results, mean, and/or median from patient samples

Establishing and refining cutoff values

Competency assessments and proficiency testing

Source: Graphic created by CDC-DLS

Quality Assurance in Newborn Screening: Post-Analytical



Reporting of results, including timeliness

Outcomes from screen-positive or screen-borderline results

Follow-up of unsatisfactory specimens

Documentation of outcomes and feedback to laboratory

Source: Graphic created by CDC-DLS

Technical Assistance: Across the System

2

Public Health Staff:

- Laboratory Methods
- Follow-Up Processes
- Data Analytics
- Troubleshooting and QA/QI

1

Birth Center Staff and Midwives:

- Specimen Collection and Transport
- Potential Result Interferences
- Parent/Guardian Education

3

Specialists and Primary Care Providers:

- Types of Screening Results
- Disease-specific Information
- Communication Resources

Source: Graphic created by CDC-DLS

Thank You

Source: Getty Stock Images, used with permission.

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
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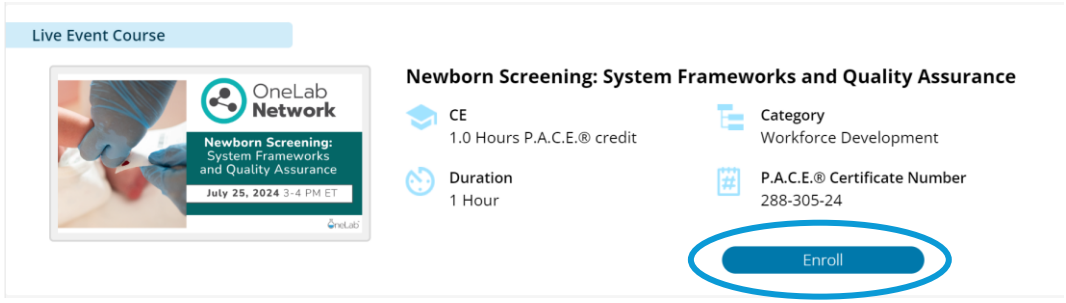
Questions?

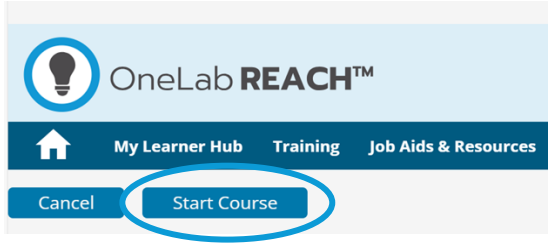
OneLab REACH™ Continuing Education

After participating in today's session, to receive continuing education credits you must:

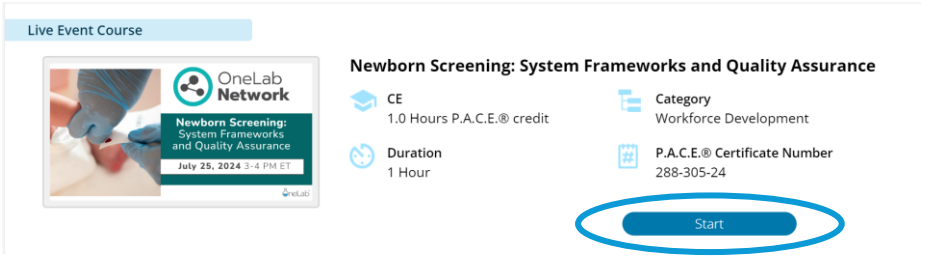
1. Log into your OneLab REACH account. **You must be logged into your REACH account to access the evaluation.**
2. Click on this link to take you to the survey.
3. Enter passcode "**V240**"
4. Click "**Enroll**"



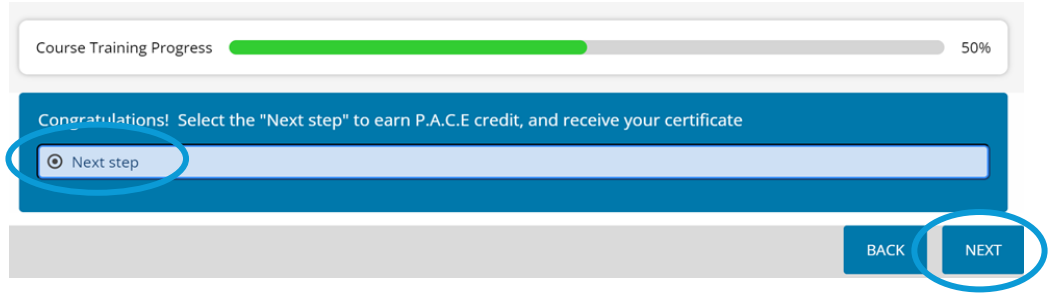
5. Select "**Start Course**".



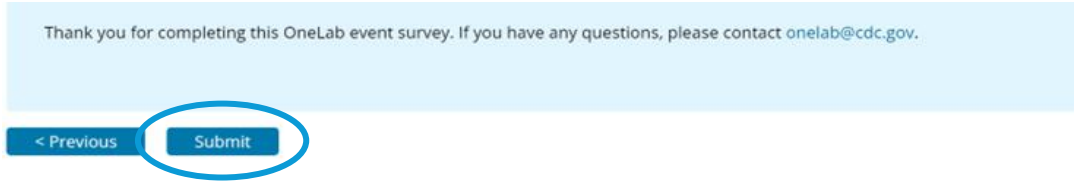
6. Select "**Start**".



7. Select "**Next step**" and "**Next**".



8. Complete the evaluation and click "**Submit**". Receive your P.A.C.E.® certificate in your MyLearnerHub.



Upcoming Event!

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