Newborn Screening

QUALITY INDICATORS

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QUALITY INDICATORS OVERVIEW

Eight newborn screening Quality Indicators are used to provide longitudinal evaluation of a newborn screening program as well as comparisons across programs. The goal of this document is to help ensure standardization of calculations and metrics across newborn screening programs.

This document provides the purpose and definition of each of the eight quality indicators as well as a glossary of terms that are used throughout the document. Additionally, Appendix B: Laboratory Information Management Systems (LIMS) Helpful Hints is included to provide you with information to aid in the extraction of the quality indicator data from the LIMS and provide guidance in instances of how to collect and report the data points.

Quality Indicator	Definition	Priority QIs for all programs	QIs for subsequent specimens	QIs for Two-screen states
QI 1	**Unsatisfactory Specimens:** Percent of dried blood spot specimens that were unacceptable due to improper collection and/or transport	1a, 1b	1c, 1d	1c, 1d
QI 2	**Missing Essential Information:** Percent of dried blood spot specimens with at least one missing essential data field upon receipt at the lab	2a	2b	2b
QI 3	**Unscreened Newborns:** Percent of newborns not receiving a newborn screen	3a		3d
QI 4	**Lost to Follow-Up:** Percent of infants that have no recorded final resolution with the newborn screening program	4a, 4b, 4c		
QI 5	**Timeliness** of newborn screening activities	5a.i, 5b.i, 5c.i, 5c.ii, 5d.i, 5d.ii, 5d.iii, 5e, 5f, 5g	5a.iii, 5b.ii, 5c.iv, 5d.iv	5a.ii, 5b.iii, 5c.v, 5d.v
QI 6	**Screen Positives:** Percent of infants with an out-of-range newborn screen result requiring clinical diagnostic workup reported by disorder or disorder category	6		
QI 7	**Confirmed Cases:** Disorders detected by newborn screening with a confirmed diagnosis by an appropriate medical professional	7a		7d
QI 8	**Missed Cases**, reported by disorder			

NewSTEPs will collect all newborn screening quality indicators (QI) but will prioritize those that the Quality Indicator Workgroup recommends for Health Resources and Services Administration (HRSA) reporting. Priority Quality Indicators are **bolded below** and represent those metrics that allow for either nationwide or programmatic longitudinal comparisons. For those programs that can submit data for all QIs, NewSTEPs will continue to support their efforts and facilitate data entry and documentation of best practices. Please direct all questions pertaining to Quality Indicators to newsteps@aphl.org.

GENERAL CONSIDERATIONS

- A **first specimen** is the earliest specimen received at the laboratory for testing. All additional specimens received at the laboratory for a given newborn are considered subsequent specimens.
- **Requested subsequent specimen** refers to any specimen received at the laboratory after the first specimen for the same newborn. A requested subsequent specimen may be received at the laboratory for:
    - An unacceptable specimen.
    - A requested repeat specimen for a borderline or out-of-range result from the first specimen.
    - A requested repeat specimen following the second screen due to borderline, out-of-range, or unacceptable second screen specimen.
    - Specimens collected as part of a routine low birth weight/premature/NICU serial screening protocol.
    - Routine second specimen refers to a second specimen collected in two-screen states, which occurs after the completion of the first mandated screen, on the same baby for routine second screening.

QUALITY INDICATOR 1 | UNSATISFACTORY SPECIMENS

a) **Percent of first dried blood spot specimens that were unacceptable due to improper collection[1,2,3] (Priority Indicator)**
b) Percent of first dried blood spot specimens that were unacceptable due to improper transport[2,4]
c) Percent of requested subsequent (including routine second) dried blood spot specimens that were unacceptable due to improper collection[1,2,3]
d) Percent of requested subsequent (including routine second) dried blood spot specimens that were unacceptable due to improper transport[2,4]

Purpose: To identify the number of dried blood spot specimens that are improperly collected or transported resulting in the need for an additional specimen collection from the newborn. This requires additional work for laboratory personnel to acquire an acceptable specimen. This metric is used for longitudinal trend analysis within the program and not for nationwide comparisons.

Screening Data used for Denominators

a-b) Number of first dried blood spot specimens received at your designated newborn screening laboratory. This includes first specimens collected from the first screen only. [5]
c-d) Number of requested subsequent dried blood spot specimens received at your designated newborn screening laboratory. This includes requested subsequent and routine second specimens (for two-screen states). [5]

Definitions

a) Number of first dried blood spot specimens on which laboratories cannot report the complete newborn screening panel due to collection errors[1,2,3], divided by the number of first dried blood spot specimens received at your designated newborn screening laboratory, multiplied by 100. This includes first specimens collected from the first screen only.[5]
b) Number of first dried blood spot specimens on which laboratories cannot report the complete newborn screening panel due to transport errors[2,4], divided by the number of first dried blood spot specimens received at your designated newborn screening laboratory, multiplied by 100. This includes first specimens collected from the first screen only.[5]
c) Number of requested subsequent dried blood spot specimens on which laboratories cannot report the complete newborn screening panel due to collection errors[1,2,3], divided by the total number of requested subsequent dried blood spot specimens received at your designated newborn screening laboratory, multiplied by 100. This includes requested subsequent and routine second specimens (for two-screen states).[5]
d) Number of requested subsequent dried blood spot specimens on which laboratories cannot report the entire newborn screening panel due to transport errors[2,4], divided by the total number of requested subsequent dried blood spot specimens received at your designated newborn screening laboratory, multiplied by 100. This includes requested subsequent and routine second specimens (for two-screen states).[5]

Footnotes

1. Do **not** include specimens with an improper time of collection (e.g., collected less than 24 hours); this is collected later in the Timeliness Quality Indicator (QI 5a). Specimens collected early per a state/territory's mandate should also be excluded from this metric.
2. If it is unknown whether unacceptable specimens were due to either improper collection or transport, they should be counted under improper collection only (QI 1a, 1c).
3. Improper collection (QI 1a, 1c) is defined as any specimen that is unacceptable for any level of testing (initial and confirmation screening) due to collection errors. Examples include:
    - Insufficient quantity of blood (QNS)
    - Clotting or smearing
    - Contamination
    - Inadequately filled circles
    - Oversaturation or layering of blood
    - Use of capillary tubes and scratching or abrading by capillary tube spotting
    - Incomplete drying before shipping
    - Specimens collected on expired dried blood spot devices
4. Improper transport (QI 1b, 1d) includes:
    - Any specimen received after the state-defined length of time from collection that deems a specimen unacceptable for testing
    - Any specimen that is damaged in transport
    - Specimens placed in an airtight or sealed plastic bag with or without a desiccant.
5. This includes multiple specimens collected from a single newborn, but not monitoring specimens (e.g., PKU monitoring).

QUALITY INDICATOR 2 |MISSING ESSENTIAL INFORMATION

a) **Percent of first dried blood spot specimens with at least one missing state-defined essential data field upon receipt at the newborn screening laboratory (Priority Indicator)** [1,2]
b) Percent of requested subsequent (including routine second) dried blood spot specimens with at least one missing state-defined essential data field upon receipt the newborn screening laboratory[1,2]

Purpose: To identify the number of submitted dried blood spot specimens missing at least one state-defined essential data field[1] upon receipt at the laboratory. This may delay the testing of a specimen and reporting of results, causing potential harm to the newborn, and requiring additional work for laboratory personnel to acquire the missing information. This metric is used for longitudinal trend analysis within the program and not for nationwide comparisons.

Screening Data used for Denominators

a) Number of first screen dried blood spot specimens received at your designated newborn screening laboratory. This includes first specimens collected from the first screen only. [3]
b) Number of requested subsequent dried blood spot specimens received at your designated newborn screening laboratory. This includes requested subsequent and routine second specimens (for two-screen states). [3]

Definitions

a) Number of first dried blood spot specimens submitted with at least one missing state-defined essential data field[1,2] upon receipt at the laboratory, divided by the number of first dried blood spot specimens received at your designated newborn screening laboratory, multiplied by 100. This includes first specimens from the first screen only. [3]
b) Number of requested subsequent dried blood spot specimens submitted with at least one missing state-defined essential data field[1,2] upon receipt at the laboratory, divided by the total number of requested subsequent dried blood spot specimens received at your designated newborn screening laboratory, multiplied by 100. This includes requested subsequent and routine second specimens (for two-screen states).[3]

Footnotes

1. Essential information is defined differently by each state/territory and consists of information that is critical for testing and follow-up activities. Missing essential information is that which impacts result interpretation and/or impedes the ability to identify and locate the infant in an emergent situation.

   The following is a list of data elements often considered essential information from the Emergency NBS Collection Devices:

   - Patient identification number
   - Infant first and last name
   - Date and time of birth
   - Date and time of specimen collection
   - Birth weight
   - Sex
   - Mother first and last name
   - Mother address
   - Mother phone
   - Submitter identification
   - Submitter address
   - Physician name
   - Physician phone

2. You do not need to tally how many fields are missing; only count the number of specimens in the numerator if at least one field is missing.
3. This includes multiple specimens collected from a single newborn, but not monitoring specimens (e.g., PKU monitoring).

QUALITY INDICATOR 3 | UNSCREENED NEWBORNS

a) **Percent of newborns without a valid dried blood screen (Priority Indicator)[1,2]**
b) Percent of newborns without a valid dried blood spot screen due to parental refusal[1]
c) Percent of newborns without a valid first dried blood spot screen due to pre-analytic error [1,2,3]
d) In two screen states, percent of newborns without a valid routine second screen due to a missing or unmatched routine second dried blood spot specimen.

Purpose: To determine the proportion of newborns that were not screened due to an invalid newborn screen, parental refusal, pre-analytic error or did not receive a routine second dried blood screen as per the recommended algorithm in that state.

Screening Data for Denominators: Number of newborns born in your state/territory. *This information is pulled from the CDC Vital Statics and does not need to be entered into the NewSTEPs Repository.*

Definitions

a) Number of newborns born in your state/territory without a valid dried blood spot screen, divided by the number of newborns born in your state/territory, multiplied by 100.[1,2]
b) Number of newborns born in your state/territory without a valid dried blood spot screen due to parental refusal, divided by the number of newborns born in your state/territory, multiplied by 100. [1]
c) Number of newborns born in your state/territory without a valid first dried blood spot screen due to pre-analytic error (e.g., specimen lost in transit, nurse forgot, newborn transferred to another hospital, unacceptable specimens that never had a subsequent specimen), divided by the number of newborns born in your state/territory, multiplied by 100.[1,2,3]
d) In two-screen states, the number of newborns born in your state/territory without a valid first and routine second screen due to a missing or unmatched dried blood spot specimen, divided by the number of newborns born in your state, multiplied by 100. [4]

Footnotes

1. Counts of unscreened newborns due to parental refusal (QI 3b) and pre-analytic error (QI 3c) should be included in the total number of unscreened newborns (QI 3a). QI 3a should be greater than or equal to QI 3b + 3c. This should not include newborns who are deceased.
2. For newborns who moved/transferred out of state prior to their newborn screen, confirm whether a newborn screen was done elsewhere before including them in the numerator.
3. This includes any pre-analytic event, except for parental refusal, that would prevent the newborn from receiving a complete screen. For dried blood spot screens, some examples include: unacceptable specimens that never had a subsequent specimen received at the laboratory, specimens lost in transit, or specimens for which hospital personnel forgot to either collect or ship the specimen.
4. This includes newborns that only received one out of the two required screens.

QUALITY INDICATOR 4 | LOST TO FOLLOW-UP

Percent of infants that have no recorded final resolution with the newborn screening program [1] by 12 months of age, following:

a) **The receipt of an unacceptable dried blood spot specimen[1] (Priority Indicator)**
b) **A borderline result for which a subsequent dried blood spot specimen was requested for repeat screening[2] (Priority Indicator)**
c) **An out-of-range result from a dried blood spot screen requiring clinical diagnostic workup by an appropriate medical professional (Priority Indicator)**

Purpose: To determine the percentage of infants that have no recorded final resolution (i.e., screening complete, confirmed diagnosis, or diagnosis ruled out by an appropriate medical professional) with the state/territorial newborn screening program, by 12 months of age, therefore, increasing the probability of harm to infants who are at-risk for a disorder on the newborn screening panel.

Screening Data for Denominators

a) Number of infants that had any unacceptable dried blood spot specimen[1]
b) Number of infants requested to have a subsequent dried blood spot specimen following a borderline result[2]
c) Number of infants with an out-of-range result from a dried blood spot screen requiring clinical diagnostic workup by an appropriate medical professional

Definitions

a) Number of infants with an unacceptable dried blood spot specimen (and no previous or later acceptable specimen) that have no recorded final resolution (i.e., screening complete) with the newborn screening program, by 12 months of age, divided by the number of infants that had any unacceptable dried blood spot specimen, multiplied by 100. [1]

b) Number of infants requested to have a subsequent dried blood specimen following a borderline result that have no recorded final resolution (i.e., confirmed diagnosis or diagnosis ruled out by an appropriate medical professional) with the newborn screening program, by 12 months of age, divided by the number of infants requested to have a subsequent dried blood spot specimen following a borderline result, multiplied by 100.[2]

c) Number of infants with an out-of-range result from a dried blood spot screen requiring clinical diagnostic workup by an appropriate medical professional, that have no recorded final resolution (i.e., confirmed diagnosis or diagnosis ruled out by an appropriate medical professional) with the newborn screening program, by 12 months of age, divided by the number of infants with an out-of-range result from a dried blood spot screen requiring clinical diagnostic workup by an appropriate medical professional, multiplied by 100.

Footnotes

1. Unacceptable dried blood spot specimens exclude those collected in less than 24 hours [for example, Neonatal Intensive Care Unit (NICU) infants].
2. In two-screen states, this does not include routine second dried blood spot specimens that are received after a first dried blood spot specimen that was negative. If no routine second screen was completed, this should be counted in Quality Indicator 3d.

QUALITY INDICATOR 5 |TIMELINESS OF NEWBORN SCREENING ACTIVITIES

Proportion of specimens that were obtained during the following process intervals:

a) Time from birth to specimen collection
b) Time from specimen collection to receipt at your designated newborn screening laboratory[1]
c) Time from specimen receipt at your designated newborn screening laboratory to reporting out specimen results to a medical provider[2]
d) Time from birth to reporting out specimen results to a medical provider[2]
e) Time from reporting out-of-range results to medical intervention by an appropriate medical professional for infants with a confirmed clinical diagnosis[2]
f) Time from birth to confirmation of clinical diagnosis by an appropriate medical professional[2]
g) For infants with an out-of-range newborn screen result requiring a clinical diagnostic workup by an appropriate medical professional, time from birth to determining if a result was a false positive

Purpose: To identify the components of the newborn screening system that can be shortened to decrease the risk of potential harm to infants who may be identified with a disorder on the newborn screening panel.

QI 5ai, bi, ci, cii, di, dii, diii, e, f and g are prioritized indicators. Please note that for QI 5g, only the denominator and total number of false positives are prioritized.

Screening Data for Denominators

a-d) The denominators for Quality Indicators 5a-d are calculated as the summation of specimens entered for each of the specified time categories. QI5a is in the unit of hours and QI5b-d are in the unit of days.

g) Number of infants that had an out-of-range dried blood spot screen result requiring clinical diagnostic workup by an appropriate medical professional.

Definitions

a) Time from birth to specimen collection with the number of specimens tallied in the following categories:

i. Number of **first** dried blood spot specimens collected in the specified time categories in units of hours <u>from birth</u>, divided by the total number of **first** dried blood spot specimens collected. Total number of first dried blood spot specimens collected is calculated through the summation of values entered for each time category.

- Less than 12 hours from birth
- 12 to 24 hours from birth
- Greater than 24 to 48 hours from birth
- Greater than 48 to 72 hours from birth
- Greater than 72 hours from birth
- Time elapsed unknown

ii. In two screen states, number of dried blood spot specimens collected for the **routine**

second screen in the following time categories in units of days from birth, divided by the total number of dried blood spot specimens collected for the **routine second screen**. Total number of dried blood spot specimens collected for the routine second screen is calculated through the summation of values entered for each time category. *This does not include requested subsequent specimens from the routine second screen. These should be counted for QI5a.iii*.

- Less than 7 days from birth
- 7 to 10 days from birth
- 11 to 14 days from birth
- 15 days or more from birth
- Time elapsed unknown

iii. Number of **requested subsequent** dried blood spot specimens collected in the specified time categories in units of days from birth, divided by the total number of **requested subsequent** dried blood spot specimens collected. Total number of requested subsequent dried blood spot specimens collected is calculated through the summation of values entered for each time category.

- Less than 7 days from birth
- 7 to 10 days from birth
- 11 to 14 days from birth
- 15 days or more from birth
- Time elapsed unknown

b) Time from specimen collection to receipt at your designated newborn screening laboratory with the number of specimens tallied in the following categories[1]:

- Same day as collection (Day 0)
- Day after collection (Day 1)
- Day 2 after collection (Day 2)
- Day 3 after collection (Day 3)
- Day 4 after collection (Day 4)
- Day 5 after collection (Day 5)
- Day 6 after collection (Day 6)
- Greater than or equal to Day 7 after collection (>=Day 7)
- Time elapsed unknown

Calculate time from collection to receipt at lab as: (RECEIPT DATE) – (COLLECTION DATE). Results will be integer values in whole units of days.

i. Number of **first** dried blood spot specimens received at your designated newborn screening laboratory[1] in the specified time categories in units of days from specimen collection, divided by the total number of **first** dried blood spot specimens received at your designated newborn screening laboratory. Total number of first dried blood spot specimens received is calculated through the summation of values entered for each

time category.

ii. Number of **requested subsequent** dried blood spot specimens received at your designated newborn screening laboratory[1] in the specified time categories in units of days from specimen collection, divided by the total number of **requested subsequent** dried blood spot specimens received at your designated newborn screening laboratory. Total number of subsequent dried blood spot specimens received is calculated through the summation of values entered for each time category.

iii. In two-screen states, number of **routine second screen** dried blood spot specimens received at your designated newborn screening laboratory[1] in the specified time categories from specimen collection, divided by the total number of **routine second screen** dried blood spot specimens received at your designated newborn screening laboratory. Total number of routine second screen dried blood spot specimens received is calculated through the summation of values entered for each time category

c) Time from specimen receipt at your designated newborn screening laboratory to reporting out results to a medical provider, with the number of specimens tallied in the following categories[2,4]:

- Same day as receipt at lab (Day 0)
- Day after receipt at lab (Day 1)
- Day 2 after receipt at lab (Day 2)
- Day 3 after receipt at lab (Day 3)
- Day 4 after receipt at lab (Day 4)
- Day 5 after receipt at lab (Day 5)
- Day 6 after receipt at lab (Day 6)
- Greater than or equal to Day 7 after receipt at lab (>=Day 7)
- Time elapsed unknown

Calculate time from receipt at lab to reporting out specimen results as: (REPORT OUT DATE) – (RECEIPT DATE). Results will be integer values in whole units of days.

i. Number of dried blood spot specimens with out-of-range results requiring clinical diagnostic workup by an appropriate medical professional, for **time critical disorders**, reported out to a medical provider in the specified time categories in units of days from specimen receipt at your designated newborn screening laboratory, divided by the total number of dried blood spot specimens with out-of-range results requiring clinical diagnostic workup by an appropriate medical professional for **time critical disorders**. Total number of dried blood spot specimens with out-of-range results requiring clinical diagnostic workup by an appropriate medical professional for time critical disorders is calculated through the summation of values entered for each time category.[2,3,4]

ii. Number of dried blood spot specimens with out-of- range results requiring clinical diagnostic workup by an appropriate medical professional, for **non-time critical disorders**, reported out to a medical provider in the specified time categories in units of days from specimen receipt at your designated newborn screening laboratory, divided by the total number of dried blood spot specimens with out-of-range results requiring clinical diagnostic workup by an appropriate medical professional **for non-time critical disorders**. Total number of dried blood spot specimens with out-of-range results requiring clinical diagnostic workup by an appropriate medical professional for non-time critical disorders, is calculated through the summation of values entered for each time category.[2,4]

iii. Number of **first** dried blood spot specimens with normal or out-of-range result for any disorder reported out to a medical provider in the specified time categories in units of days from specimen receipt at your designated newborn screening laboratory, divided by the total number of **first** dried blood spot specimens with a normal or out-of-range result for any disorder. Total number of first dried blood spot specimens with a normal or out- of-range result for any disorder is calculated through the summation of values entered for each time category.[2,4]

iv. Number of **requested subsequent** dried blood spot specimens with a normal or out-of-range result for any disorder reported out to a medical provider in the specified time categories in units of days from specimen receipt at your designated newborn screening laboratory, divided by the total number of **requested subsequent** dried blood spot specimens with a normal or out-of- range result for any disorder. Total number of requested subsequent dried blood spot specimens with a normal or out-of-range result for any disorder is calculated through the summation of values entered for each time category.[2,4]

v. In two screen states, number of **routine second** dried blood spot specimens with a normal or out-of-range result for any disorder reported out to a medical provider in the specified time categories in units of days from specimen receipt at your designated newborn screening laboratory, divided by the total number of **routine second** dried blood spot specimens with a normal or out-of-range result for any disorder. Total number of routine second screen dried blood spot specimens with a normal or out-of-range result for any disorder is calculated through the summation of values entered for each time category.

d) Time from birth to reporting out specimen results to a medical provider, with the number of specimens tallied in the following categories[2,4]:

- Less than or equal to Day 2 after birth (<=Day 2)
- Day 3 after birth (Day 3)
- Day 4 after birth (Day 4)
- Day 5 after birth (Day 5)
- Day 6 after birth (Day 6)
- Day 7 after birth (Day 7)
- Day 8 after birth (Day 8)

- Day 9 after birth (Day9)
- Greater than or equal to Day 10 after birth (>=Day 10)
- Time elapsed unknown

Calculate time from birth to reporting out specimen results as: (REPORT OUT DAY) – (BIRTH DATE). Results will be integer values in whole units of days.

i. Number of dried blood spot specimens with out-of-range results requiring clinical diagnostic workup by an appropriate medical professional, for **time critical disorders**, reported out to a medical provider in the specified time categories in units of days from birth, divided by the total number of dried blood spot specimens with out-of-range results requiring clinical diagnostic workup by an appropriate medical professional for **time critical disorders**. Total number of dried blood spot specimens with out-of-range results requiring clinical diagnostic workup by an appropriate medical professional for time critical disorders is calculated through the summation of values entered for each time category.[2,3,4]

ii. Number of dried blood spot specimens with out-of- range results requiring clinical diagnostic workup by an appropriate medical professional, for **non-time critical disorders**, reported out to a medical provider in the specified time categories in units of days from birth, divided by the total number of dried blood spot specimens with out-of-range results requiring clinical diagnostic workup by an appropriate medical professional for **non-time critical disorders**. Total number of dried blood spot specimens with out-of-range results requiring clinical diagnostic workup by an appropriate medical professional for non-time critical disorders is calculated through the summation of values entered for each time category.[2,4]

iii. Number of **first** dried blood spot specimens with a normal or out-of-range result for any disorder reported out to a medical provider in the specified time categories in units of days from birth, divided by the total number of **first** dried blood spot specimens with a normal or out-of-range result for any disorder. Total number of first dried blood spot specimens with a normal or out-of-range result for any disorder is calculated through the summation of values entered for each time category.[2,4]

iv. Number of **requested subsequent** dried blood spot specimens with a normal or out-of-range result for any disorder reported out to a medical provider in the specified time categories in units of days from birth, divided by the total number of **requested subsequent** dried blood spot specimens with a normal or out-of-range result for any disorder. Total number of requested subsequent dried blood spot specimens with a normal or out-of-range result for any disorder is calculated through the summation of values entered for each time category.[2,4]

v. In two screen states, number of **routine second** dried blood spot specimens with a

normal or out-of-range result for any disorder reported out to a medical provider in the specified time categories in units of days from birth, divided by the total number of **routine second** dried blood spot specimens with a normal or out-of-range result for any disorder. Total number of routine second screen dried blood spot specimens with a normal or out-of-range result for any disorder is calculated through the summation of values entered for each time category.

e) **Time from reporting out-of-range results requiring clinical diagnostic workup by an appropriate medical professional to medical intervention [2,4] for infants with a confirmed clinical diagnosis.** QI 5e requires infants with a confirmed clinical diagnosis to be entered as an individual case in the NewSTEPs Repository with time from reporting out-of-range results to intervention by a medical professional entered in units of days. A table for QI 5e is automatically generated that pulls and aggregates necessary case data from the NewSTEPs Repository. All information in this table is reported by disorder or disorder category. [5]

f) **Time from birth to confirmation of clinical diagnosis.** QI 5f requires infants with a confirmed clinical diagnosis to be entered as an individual case in the NewSTEPs Repository with time from birth to confirmed clinical diagnosis entered in units of days.[2] A table for QI 5f is automatically generated that pulls and aggregates necessary case data from the NewSTEPs Repository. All information in this table is reported by disorder or disorder category.[5]

g) **For infants with an out-of-range newborn screen result requiring a clinical diagnostic workup by an appropriate medical professional, time from birth to determining if a result was a false positive result[6], with the number of false positives tallied in the following categories, reported by disorder category.[5]**

Please note that for QI 5g, only the denominator and total number of false positives are prioritized.

- Total number of analytical false positives called out
- No false positives called out
- Less than 7 days after birth
- 7-14 days after birth
- 15 days to 1 month after birth
- Greater than 1 month to 2 months after birth
- Greater than 2 months to 6 months after birth
- Greater than 6 months to 9 months after birth
- Greater 9 months to 12 months after birth
- Greater than 12 months after birth
- Time elapsed unknown

Number of infants requiring clinical diagnostic workup by an appropriate medical professional due to an out-of-range result from the dried blood spot screen determined to be a false positive result[6] in the specified time intervals from birth, reported by disorder category[5],

divided by the number of infants that had an out-of-range result from a dried blood spot screen requiring clinical diagnostic workup by an appropriate medical professional, multiplied by 100.

Quick Tips

- Time from birth to collection (QI5a) is the only measure collected in the unit of hours. All other measures (QI 5b-g) are collected in the unit of days (i.e., will be an integer in units of whole days).
- Each quality indicator has a designated measure for first, requested subsequent and routine second specimens. Please ensure that you separate out these screens and enter them in the appropriate fields.
- For time critical disorders (QI5c.i, QI5d.i) and non-time critical disorders (QI5c.ii and QI5d.ii), NewSTEPs does not specify whether these measures should include first specimens, requested subsequent specimens, or routine second specimens. The purpose of this quality indicator is to capture the time it takes to interpret the actionable result or act on that result. For this measure, time intervals should be calculated using the report-out times for the earliest specimen tested that detected the borderline or out-of-range result that led to an infant seeking diagnostic work-up by a medical professional.
    - Calculate time to report out using the **first specimen** if:
        - An out-of-range result was detected on the first specimen
        - An out-of-range result was detected on the first specimen and confirmed on the requested subsequent specimen.
        - A borderline result was detected on the first specimen and an out-of-range result was detected on the requested subsequent specimen during repeat testing
        - A first specimen was unsatisfactory, *tested*, and detected the out-of-range result (i.e., unsatisfactory first specimen detected an out-of-range result)
    - Calculate the time to report out using the **requested subsequent specimen** if the first specimen was unsatisfactory, not tested, and the resulting requested subsequent specimen detected an out-of- range result during repeat testing.
    - For **two-screen states**, calculate the time to report out using the specimen from which the out-of-range result was detected.

Footnotes

1. In the NewSTEPs Repository, state/territory profiles gather information on how newborn screening programs define receipt at laboratory and how this is recorded.
2. See Definitions for Medical Intervention and Diagnosis
3. Time Critical Disorders: The following table is from the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children's (ACHDNC) recommendations on timeliness in newborn screening and was created based on the Society for Inherited Metabolic Disorders

(SIMD) position statement and expert opinion from metabolic geneticists, hematologists, endocrinologists, and pulmonologists.

Organic Acid Conditions	Fatty Acid Oxidation Disorders	Amino Acid Disorders	Endocrine Disorders	Other Disorders
Propionic acidemia (PROP)	Medium-chain acyl-CoA dehydrogenase deficiency (MCADD)	Argininosuccinic aciduria (ASA)	Congenital adrenal hyperplasia (CAH)	Classic galactosemia (GALT)
Methylmalonic acidemia (methylmalonyl-CoA mutase) (MUT)	Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)	Citrullinemia, type I (CIT)		Glycogen Storage Disorder, type II (Infantile Pompe)
Isovaleric acidemia (IVA)	Long-chain L-3 hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)	Maple syrup urine disease (MSUD)		Infantile Krabbe Disease
3-Hydroxy-3-methyglutaric aciduria (HMG)	Trifunctional protein deficiency (TFP)			
Holocarboxylase synthase deficiency (MCD)	Glutaric acidemia, type II (GA II)			
β-Ketothiolase deficiency (BKT)	Carnitine acylcarnitine translocase deficiency (CACT)			
Glutaric acidemia, type I (GA I)	Carnitine palmitoyltransferase type II deficiency (CPT II)			

4. For time to report out, the report-out date should be when a medical provider is notified (in the case of actionable results) and when the report is released back to the submitter for normal results.
5. Medical Intervention**:** Any interaction by a medical professional with the infant's family that changes the current care for the infant based on the newborn screening results and/or the presumptive diagnosis for a specific disorder. Intervention may occur in a medical setting or may include changes in care per phone conversations. Examples include advising parents to not let a newborn fast following an out-of-range MCADD newborn screen or initiating antibiotic therapy in the case of an out-of-range sickle cell newborn screen. Medical intervention may precede a formal diagnosis and does not include additional newborn screen specimen collection (Appendix A: Glossary of Terms).
6. Disorder categories and the disorders they encompass are found here: Recommended Uniform Screening Panel | HRSA
7. A false positive is a screen positive result indicating that an individual is at increased risk for the primary target disease when the individual is found later to be unaffected. This includes infants that are truly unaffected, as well as infants that had a non-target, but clinically relevant finding (e.g., carriers, pseudodeficiencies, CRMS, etc.)

QUALITY INDICATOR 6 | SCREEN POSITIVES

Percent of newborns with an out-of-range result from the dried blood spot screen requiring clinical diagnostic workup by an appropriate medical professional, reported by disorder or disorder category[1,2] (Priority Indicator)

Purpose: To determine the percentage of newborns with an out-of-range newborn screen result requiring further clinical diagnostic workup by a health care professional, reported by disorder or disorder category.[1]

Screening Data for Denominator
Number of newborns, born in your state/territory that received a dried blood spot screen whose specimen was received at your designated newborn screening laboratory.[3]

Definition
Number of newborns with an out-of-range result from the dried blood spot screen requiring clinical diagnostic workup by an appropriate medical professional, reported by disorder or disorder category,[1,2] divided by the number of newborns, born in your state/territory that received a dried blood spot screen whose specimen was received at your designated newborn screening laboratory [3], multiplied by 100.

Footnotes

1. The breakout of disorders and disorder categories are:
    - Organic Acid Disorders
    - Fatty Acid Disorders
    - Amino Acid Disorders
    - Endocrine Disorders
        - Congenital adrenal hyperplasia (CAH)
        - Congenital hypothyroidism (CH)
    - Hemoglobin Disorders
    - Lysosomal Storage Disorders
        - Mucopolysaccharidosis I (MPS I)
        - Mucopolysaccharidosis II (MPS II)
        - Pompe
    - Other Disorders
        - Biotinidase deficiency (BIOT)
        - Cystic Fibrosis
        - Classic Galactosemia (GALT)
        - Guanidinoacetate methyltransferase deficiency (GAMT)
        - Severe combined Immunodeficiencies (SCID)
        - X-linked Adrenoleukodystrophy (XALD)
        - Spinal Muscular Atrophy (SMA)
2. If your NBS program is not screening for a particular disorder, please leave blank and do not enter zero as this affects the data quality.
3. All newborns for whom a specimen was received, whether acceptable or unacceptable should be included in this count. This does not include refusals, deaths, or blank collection devices.

QUALITY INDICATOR 7 | CONFIRMED CASES

a) **Birth prevalence of disorders detected by newborn screening with a confirmed diagnosis by an appropriate medical professional, reported by disorder[1,2] (Priority Indicator)**
b) Number of infants detected from the first dried blood spot specimen with a confirmed diagnosis by an appropriate medical professional, reported by disorder[1]
c) Number of infants detected from the requested subsequent dried blood spot specimen with a confirmed diagnosis by an appropriate medical professional, reported by disorder[1]
d) In two-screen states, number of infants detected by the routine second dried blood spot specimen (or subsequent specimen requested after the routine second specimen) with a confirmed diagnosis by an appropriate medical professional, reported by disorder[1]

Purpose: To determine the birth prevalence of each disorder detected by newborn screening for each state/territory.

Definitions: Quality Indicator 7 requires infants with a confirmed diagnosis of a newborn screening disorder to be entered as a case in the NewSTEPs Repository.[1]

a) Number of infants with an out-of-range result from any dried blood spot specimen and with a confirmed diagnosis of a disorder on your state/territory's newborn screening panel by an appropriate medical professional, reported by disorder.[1,2]
b) Number of infants with an out-of-range result from the first dried blood spot specimen, requiring clinical diagnostic workup, and with a confirmed diagnosis of a disorder on your state/territory's newborn screening panel by an appropriate medical professional, reported by disorder.[1]
c) Number of infants with an out-of-range result from a requested subsequent dried blood spot specimen, requiring clinical diagnostic workup, and with a confirmed diagnosis of a disorder on your state/territory's newborn screening panel by an appropriate medical professional, reported by disorder.[1]
d) In two screen states, number of infants with an out-of-range result from the routine second screen that did not have an out-of-range result from the first screen, requiring clinical diagnostic workup and with a confirmed diagnosis of a disorder on your state/territory's newborn screening panel by an appropriate medical professional, reported by disorder.[1]

Footnotes

1. Quality Indicator 7a is pulled from NewSTEPs' aggregate cases and QI 7b-d is pulled from the individual cases as we need the screening information to determine which screen the case was identified.
2. Total confirmed cases (QI 7a) are intended to be the summation of confirmed cases identified by the first (QI7b), requested subsequent (QI7c), and routine second (QI7d) screens.

QUALITY INDICATOR 8 | MISSED CASES

a) Number of infants that have a confirmed diagnosis by a physician but did not have an out-of-range newborn screen result on their valid dried blood spot screen, reported by disorder [1,2,3]
b) Number of infants that have a confirmed diagnosis by a physician but did not have an out-of-range newborn screen result because they did not have a valid dried blood spot screen due to error, reported by disorder[1,2,3]

Purpose: To describe how accurately newborn screening programs are identifying infants with each disorder.

Definitions: Quality Indicator 8 requires infants with a confirmed diagnosis of a newborn screening disorder on your state/territory's newborn screening panel to be entered as an individual case in the NewSTEPs Repository.

a) Number of infants with a confirmed diagnosis by a physician for a specific newborn screening disorder but did not have an out-of-range screen result on a valid dried blood spot screen, by disorder.[1,2,3]
b) Number of infants with a confirmed diagnosis by a physician for a specific newborn screening disorder but did not have an out-of-range screen result because they did not have a valid dried blood spot screen due to error, by disorder.[1,2,3]

Footnotes

1. This is the number of missed cases known by the state/territory. A missed case is only considered to be missed if your state/territory was screening for that disorder at the time of birth. NewSTEPs State Profile capture how the NBS program collects information on missed cases (i.e., active surveillance vs. passive surveillance).
2. Follow-up time for missed cases is up to 18 years of age.
3. This is pulled from the individual case entry, where the question "was this individual diagnosed later in life (not identified by newborn screening)?" is selected as Yes.

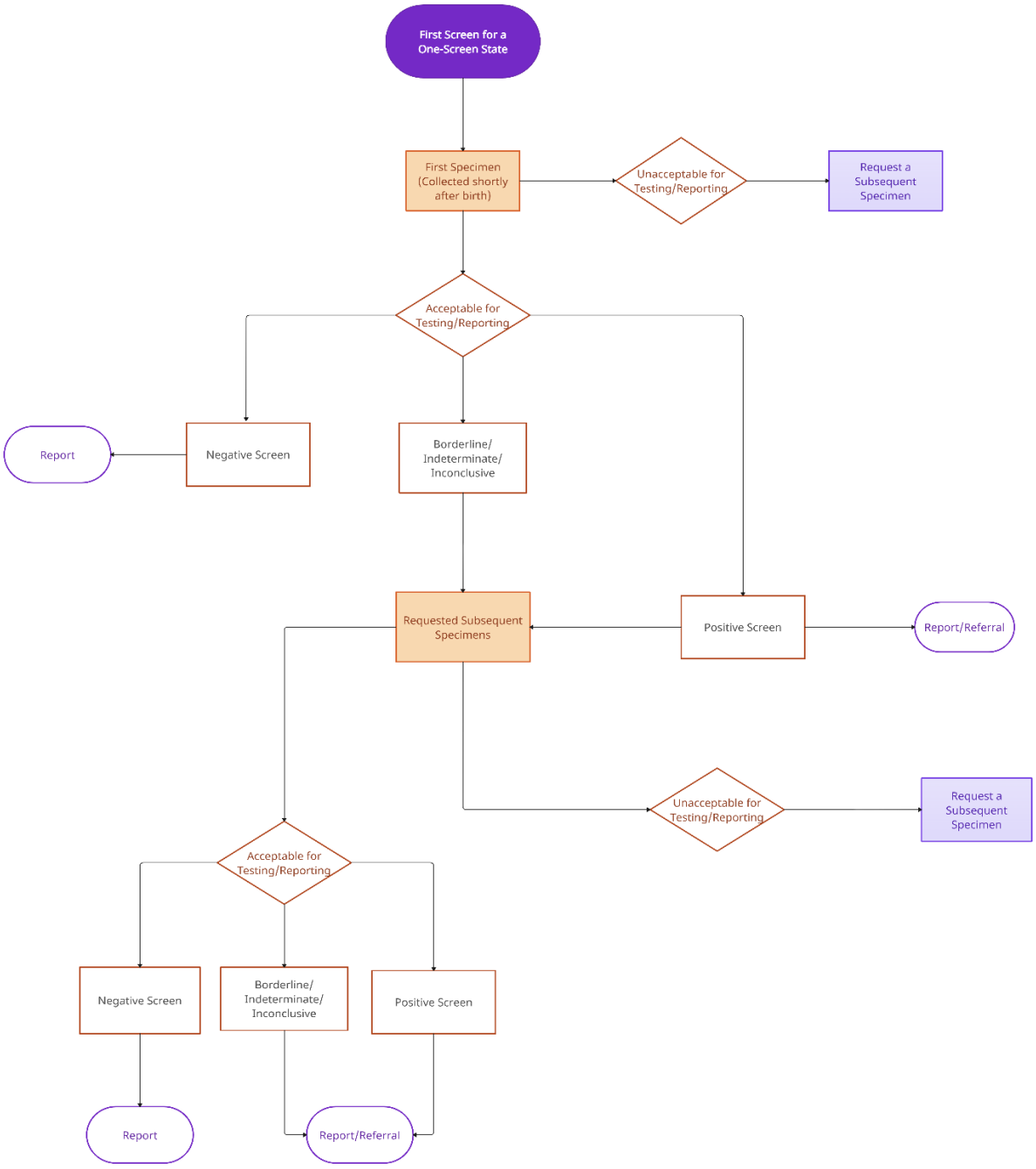
APPENDIX A | GLOSSARY OF TERMS

- **Borderline Results:** Results derived from the testing of a dried blood spot newborn specimen that require the request of a subsequent dried blood spot specimen for repeat testing.

- **Disorder Categories:** Quality Indicators 5e-f and 6 are reported by disorder category. Disorder categories and the disorders they encompass are found here: Recommended Uniform Screening Panel | HRSA.

- **Essential Information:** Essential information is defined differently by each state/territory and consists of information that is critical for specimen testing and follow-up activities. Missing essential information is that which will require additional work by lab staff to obtain. The following is a list of data elements considered essential information from the Emergency NBS Collection Devices:[1]
  - Patient Identification Number
  - Infant's First Name
  - Infant's Last Name
  - Date of Birth
  - Time of Birth
  - Date of Specimen Collection
  - Time of Collection
  - Birth Weight
  - Sex
  - Mother's First Name
  - Mother's Last Name
  - Mother's Address
  - Mother's Phone
  - Submitter Identification
  - Submitter's Address
  - Physician's Name
  - Physician's Phone

- **False Positive:** A false positive is a screen positive result indicating that an individual is at increased risk for the primary target disease when the individual is found later to be unaffected. This includes infants that are truly unaffected, as well as infants that had a non-target, but clinically relevant finding (e.g., carriers, pseudodeficiencies, CRMS, etc.)
- **First Screen:** For two screen states, the first screen is the dried blood spot screen performed on the newborn based on the specimen collected closest to the time of birth, but not exceeding the state-defined timeline for the second screen (mandated or not). States without a second screen (mandated or not), can only have a first screen.



- **First Specimen:** The earliest specimen received at the laboratory for a dried blood spot newborn screen. A first specimen can only be received at the laboratory once per screen. All additional specimens received at the laboratory for a given newborn screen are considered subsequent specimens.

- **Improper Collection**: Any specimen that is unacceptable for testing due to collection errors. Examples of improper collection are unacceptable dried blood specimens with insufficient

quantity of blood, clotting, smearing or contamination (water, feeding formulas, antiseptic solutions, or powder from gloves or other materials); inadequately filled circles; oversaturation with blood; scratching or abrading by capillary tube spotting; incomplete drying before mailing; and specimens collected on expired dried blood spot devices. Improper collection is defined by Clinical and Laboratory Standards Institute (CLSI).[2]

- **Improper Transport:** Any specimen received after the state-defined length of time that deems a specimen unacceptable for testing. Any specimen that is damaged in transport (crushed, exposed to water or other liquid, torn, etc.) or specimens placed in a sealed plastic bag without a desiccant should also be considered improper transport. Improper collection is defined by Clinical and Laboratory Standards Institute (CLSI).[2]

- **Infant:** A baby who is greater than or equal to one month of age and less than 12 months of age.

- **Medical Intervention:** Any interaction by a medical professional with the infant's family that changes the current care for the infant based on the newborn screening results and/or the presumptive diagnosis for a specific disorder. Intervention may occur in a medical setting or may include changes in care per phone conversations. Examples include advising parents to not let a newborn fast following an out-of-range MCADD newborn screen or initiating antibiotic therapy in the case of an out-of-range sickle cell newborn screen. Medical intervention may precede a formal diagnosis and does not include additional newborn screen specimen collection.

- **Monitoring Specimens:** Specimens that are collected and tested throughout the lifespan of an individual with a confirmed diagnosis of a disorder on the newborn screening panel for the purpose of managing and monitoring the severity of the disorder. An example of this is the testing of phenylalanine levels in individuals diagnosed with PKU for the purpose of dietary management.

- **Newborn:** A young child less than one month of age.

- **Out-of-Range Results:** Results derived from a dried blood spot or point-of-care screen that require further clinical diagnostic workup by an appropriate medical provider.

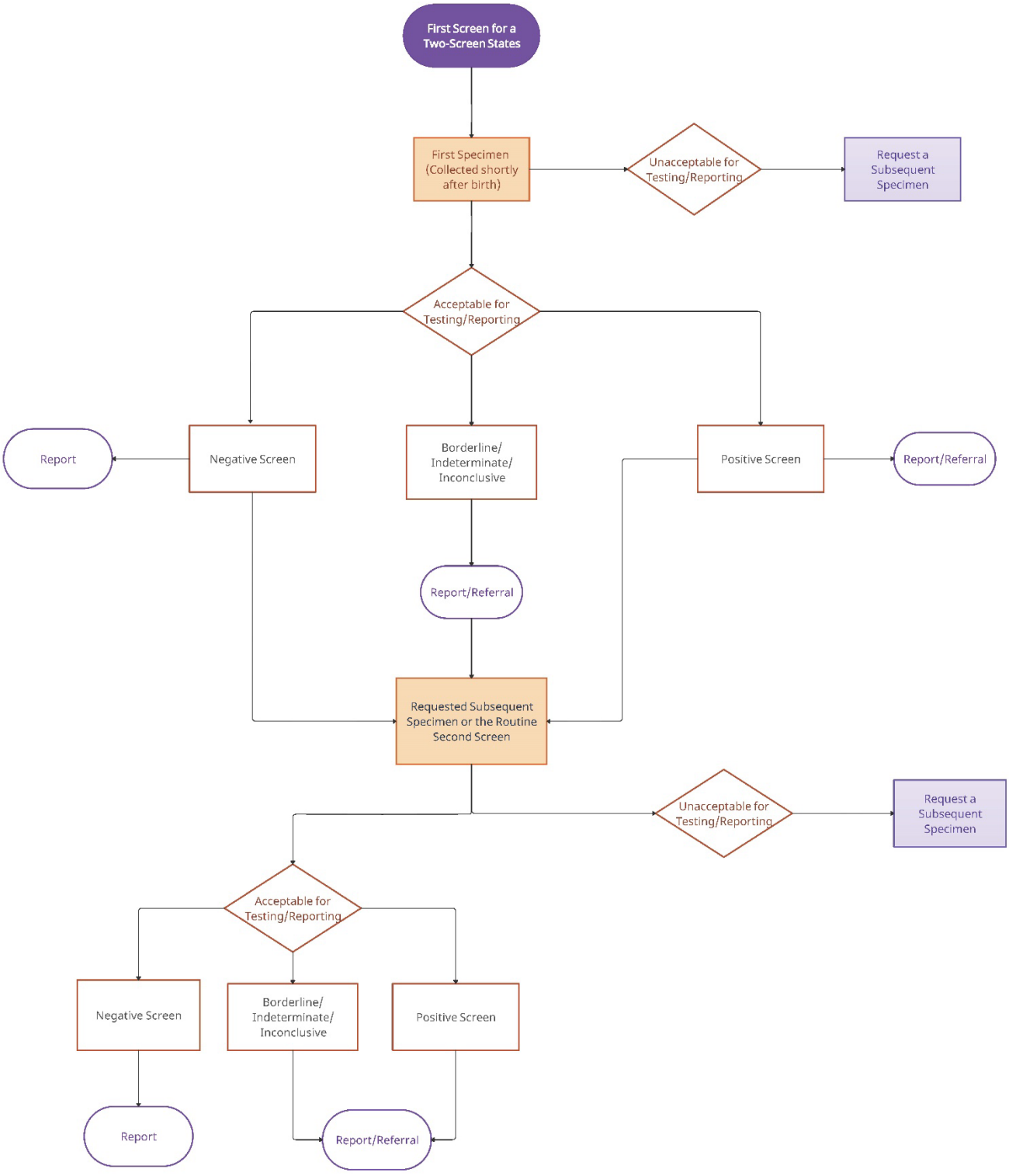
- **Repeat Testing:** A requested subsequent specimen for the purpose of retesting a sample to verify a borderline result from the first specimen for any given newborn screen.

- **Pre-Analytic Error:** Any error occurring prior to the specimen being received at the laboratory that would prevent the newborn from receiving a complete screen using that specimen. For dried blood spot screens, some examples include: unacceptable specimens that never had a subsequent specimen received at the laboratory; specimens lost in transit; or specimens for which hospital personnel forgot to either collect or ship the

specimen.

- **Sample:** In newborn screening, a sample is taken from a newborn's blood specimen via hole-punch and tested for any of the disorders on the newborn screening panel. Multiple samples may be taken and tested from one specimen.

- **Second Screen:** For two screen states, the routine second screen is the dried blood spot screen performed on the newborn collected closest to the state defined deadline for the second screen and occurring after the completion of the first mandated screen. The routine second screen may encompass the first specimen collected for the second screen, and any requested subsequent specimens collected for the second screen due to a borderline out-of-range result or unacceptable specimen.



- **Second Specimen:** refers to a routine second specimen collected in two- screen states, which occurs after the completion of the first mandated screen and performed on the same

newborn within the state/territory deadline for the routine second screen.

- **Specimen:** In newborn screening, blood drawn from a newborn and placed on a newborn screening card is referred to as a specimen. The blood is referred to as a specimen for the remainder of its existence on the newborn screening card. A sample is then taken from the specimen via hole-punch and tested. Multiple samples may be taken and tested from one specimen.

- **Subsequent Specimen:** Any specimen received at the laboratory for a given newborn screen after the first specimen has been received at the laboratory for the same newborn screen. A requested subsequent specimen may be received at the laboratory based on a borderline or inconclusive result from the first specimen, or an unacceptable first specimen. There may be multiple requested subsequent specimens per screen.

Footnotes

1. Emergency NBS Collection Cards: The card and associated data collection form were designed by the Quality Assurance/Quality Control (QA/QC) Subcommittee of the Newborn Screening Committee of APHL. The blood collection cards are housed at the Newborn Screening Quality Assurance Program (NSQAP), Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. NSQAP will be responsible for assuring the performance (i.e., expiration date) of the filter paper during card storage at CDC)
2. Blood Collection on Filter Paper for Newborn Screening Programs; Approved Standard—Fifth Edition. CLSI document LA4-A5 (ISBN 1-56238-644-1). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2007).

APPENDIX B | LABORATORY INFORMATION MANAGEMENT SYSTEM (LIMS) HINTS

Annual Measurement Point of Reference: For the purposes of manually entering or uploading quality indicator data into the NewSTEPs Repository, data will need to be pulled and aggregated from your laboratory and follow-up information systems on an annual basis. The annual time interval used for aggregating data is January 1 – December 31 of each year. If the quality indicator refers to specimens, then all specimens that were received at the laboratory between January 1 and December 31 of the given year should be included in the calculation. If the quality indicator refers to infants, then all infants born between January 1 and December 31 of the given year should be included in the calculation.

For example, a baby in your state/territory was born on December 30, 2012, and the dried blood spot specimen for this newborn was received at your newborn screening laboratory on January 1, 2013. For all quality indicators using specimens as the unit of measurement, this newborn's specimen would be included in your summation of specimens for the year 2013, even though the baby was born in the year 2012. For all quality indicators using newborns or infants as the unit of measurement, this newborn would be included in your summation of newborns or infants for the year 2012, even though the dried blood spot specimen was received in the year 2013.

The quality indicators that measure specimens and, therefore, use the date the specimen was received at the laboratory as the annual measurement point of reference are:

- Quality Indicators: 1 (a-b), 2, and 5 (a-d)

The quality indicators that measure newborns or infants and, therefore, use the date of birth as the annual measurement point of reference are:

- Quality Indicators: 3 (a-e) 4 (a-d), 5 (e-g), 6, 7 (a-d), and 8 (a-b)

Quality Indicator 1: Any specimens that were unacceptable due to both improper collection and transport should be counted under improper collection only. If it is unknown whether unacceptable specimens were due to either improper collection or transport, they should be counted under improper collection only. Categories used by your newborn screening program for improper collection and improper transport should be communicated to your LIMS vendor, where applicable.

Quality Indicator 2: State-defined essential information that is missing or incorrect is likely to be corrected within LIMS, resulting in the inability to quantify the missing or incorrect data elements. It is recommended that newborn screening programs flag data elements in their LIMS that are initially missing data, as well as tag updated fields with a time stamp to ensure that all data fields initially missing essential information can be tracked. Additionally, the data fields considered essential information should be communicated to your LIMS vendor, where applicable.

Quality Indicator 3: LIMS systems may not be able to count subsequent specimens if a link does not exist to connect the first specimen with any subsequent specimens for the same newborn. It is recommended that all specimens be matched to a newborn using a universal identifier within the LIMS, and across information systems within the newborn screening laboratory. For two-screen states, it may be helpful to include a checkbox on the newborn screening card with a corresponding variable in the LIMS that indicates whether a specimen is a first specimen, subsequent specimen, or a specimen from a second screen.

Quality Indicator 4: There is complexity with combining data from lab and follow-up information systems. If your state/territory uses the same vendor for both, it is recommended to work with the vendor to develop queries to combine necessary data elements for reporting for Quality Indicator 4. If your state/territory uses a separate vendor for lab and follow-up information systems, we recommend that each vendor work to together to aggregate the data for the purposes of reporting quality indicator data. If this situation applies to your state/territory, please contact NewSTEPs for more information.

Quality Indicator 5: Updated Categories in Units of Days:

Quality Indicator	(Date – Date) Value	New Category	Reference Date
QI5b (All): Collection to Receipt	0	Same Day (Day 0)	Calendar Day of Collection
	1	Next Day (Day 1)	Calendar Day of Collection
	2	Day 2	Calendar Day of Collection
	3	Day 3	Calendar Day of Collection
	4	Day 4	Calendar Day of Collection
	5	Day 5	Calendar Day of Collection
	6	Day 6	Calendar Day of Collection
	>6	>= Day 7	Calendar Day of Collection
	Missing/invalid	Unknown	Calendar Day of Collection
QI5c (All): Receipt to Reporting	0	Same Day (Day0)	Calendar Day of Receipt at the Lab
	1	Next Day (Day 1)	Calendar Day of Receipt at the Lab
	2	Day 2	Calendar Day of Receipt at the Lab
	3	Day 3	Calendar Day of Receipt at the Lab
	4	Day 4	Calendar Day of Receipt at the Lab
	5	Day 5	Calendar Day of Receipt at the Lab
	6	Day 6	Calendar Day of Receipt at the Lab
	>6	>= Day 7	Calendar Day of Receipt at the Lab
	Missing/invalid	Unknown	Calendar Day of Receipt at the Lab

CHANGE LOG

Modifications made from March 24, 2022 version

- Prioritized Quality Indicators have been highlighted
- **Quality Indicator 3:** eligible births removed from denominator language, requesting only number of newborns born in your state/territory.
    - Note: Due to limited linkages to vital records, most NBS programs are unable to provide eligible births at this time. With consultation from the QI workgroup, the denominator was changed to collect all newborns, while the numerator remains the same.
- **Quality Indicator 4b:** denominator changed from "*Number of infants in the state requested to have a subsequent dried blood spot specimen for repeat testing following a borderline result from the first dried blood spot specimen*" to "*Number of infants in the state/territory requested to have a subsequent dried blood spot specimen for repeat testing following a borderline result.*"
- **Quality Indicator 5g**: Added category for "total number of analytical false positives called out"

Modifications made from May 24, 2022 version

- Appendix A "disorder categories" replaced with link to HRSA RUSP.

Modifications made from October 4, 2022 version

- **Quality Indicator 5**
    - Updated purpose statement so it is clearer.
    - Removed following statement from footnote 1: Recording of Specimen receipt by lab: a) Date and time stamp (gold standard); b) Date stamp; c) Other, please describe.

Modifications made from December 6, 2022 version

- Removed footnote 3 from definition of QI3e
- Added the following language to QI3e: "have not received the following screens"
- For the definition of 3ci added the example of "unacceptable specimens that never had a subsequent specimen"
- For the definitions of 3cii and 3ciii added the examples of "malfunctioning equipment, child discharged prior to screen or misinterpretation of the point-of-care algorithm"
- Removed footnote 3 from QI 4b

Modifications made from March 2, 2023 version

- For essential information (QI 2), changed from *birth weight at time of specimen collection* to *birth weight*
- Updated the table of Time Critical Disorders (footnote of QI 5) to include secondary conditions (GA II, CPT II and CACT).

- The denominator, number of newborns born in your state/territory (QI 3 and 8b) will be pulled from the CDC Vital statics and no longer needs to be entered into the NewSTEPs Repository.
- For Quality Indicator 3, added a new footnote to clarify that counts of unscreened newborns due to refusal (3b) and pre-analytic error (3c) should be included in the total number of unscreened newborns (3a).

Modifications made from April 13, 2023 version

- At this time, NewSTEPs will no longer collect point-of-care screens (CCHD, EHDI) for quality indicator purposes; these have been removed from the source document, upload files, and online form.
    - CCHD quality indicators that have been removed include: 3a.ii, 3b.ii, 3c.ii, 3e.ii, 4d, 5a.ii, 6b
    - EHDI quality indicators that have been removed include: 3a.iii, 3b.iii, 3c.iii, 3e.iii, 4e, 5a.iii, 6c
    - Please note that this impacts the ordering for QI 5a where time to collection for routine second screens is now QI 5a.ii (used to be QI 5a.iv) and time of collection for requested subsequent specimens is now QI 5a.iii (used to be QI5a.v).
- Throughout the document, we updated language for subsequent and second specimens so it is aligned with CLSI. These are now referred to as *requested* subsequent specimens and *routine* second specimens.
- Stratified first and requested subsequent (including routine second) specimens for unsatisfactory specimens (QI 1) and missing essential information (QI 2); QI 1c, 1d and 2b have been added to distinguish between first and requested subsequent specimens.
- Updated language for Quality Indicator 3d to better clarify the number of infants in a two-screen state that did not receive the first or second screen. This could be a result of the NBS program not receiving the second screen or a result of an unmatched screen.
- Removed Quality Indicator 3e: *"Within states/territories that link newborn screening results to the electronic birth certificate/vital records, the percent of newborns that have not received a valid newborn screen."* We decided to no longer collect this information because it is redundant to QI 3a (percent of infants with an invalid dried blood spot screen) and can infer that QI 3a should equal QI 3e if NBS programs are able to link this to electronic birth certificates/vital records.
- Added a quality indicator to measure the transport time of routine second specimens (QI 5b.iii).
- For time to report out (QI5c and QI 5d), clarified that the report out date should be when a medical provider is notified (in the case of actionable results) and when the report is released back to the submitter for normal results (QI 5c.iii and QI5d.iii).
- Added a definition for false positives (Quality Indicator 5g); this has also been added to Appendix A: Glossary of Terms. A false positive is a screen positive result indicating that an individual is at increased risk for the primary target disease when the individual is found later to be unaffected. This includes infants that are truly unaffected, as well as

infants that had a non-target, but clinically relevant finding (e.g., carriers, pseudodeficiencies, CRMS, etc.)

- Removed denominator collection for confirmed cases (Quality Indicator 7) as prevalence will be determined by annual births.
- Removed denominator collection for missed cases (Quality Indicator 8) as the number of missed cases is so small compared the denominators collected (i.e., total number of cases and number of infants born in your state), which would result in an extremely small percentage.
- Updated diagrams for the first and second screen definitions in the Appendix.

Modifications made from March 20, 2024 version

- Glycogen storage disorder, type II (infantile pompe) was added to the time-critical disorder table.

Modifications made from July 12, 2024 version

- Infantile Krabbe Disease was added to the time-critical disorder table.