# INITIAL STATEMENT OF REASONS (ISOR)

## Purpose and Objectives

The Newborn Screening (NBS) Program, located in the California Department of Public Health (Department), is submitting a package of proposed regulatory changes to clarify and make specific Health and Safety Code sections 124977 and 125001 and update the newborn screening regulations in order to protect the health, and prevent unnecessary death of, newborns born in California. The proposed regulations incorporate necessary changes in the NBS requirements for newborn's physicians, midwives, perinatal health facilities/hospitals, and other out-of-hospital newborn screening providers as a result of the following:

1. Expansion of Newborn Screening which occurred in 2005 and 2007, resulting in a substantial increase in the number of disorders for which newborns are tested. The testing panel has grown from four (4) tests detecting 29 diverse disorders to eight (8) tests detecting 80 diverse disorders. (See "Problem Statement Overview and Background" below and attached list of Disorders Detectable by NBS Program as of January 1, 2012.)

2. Expansion in 2012 to include testing for an additional disorder - Severe Combined Immunodeficiency (SCID).

3. Changing technology, terminology, medical standards, and practices that have occurred in the field of newborn screening internationally, nationally, and in California since the last NBS regulations were written.

The proposed regulations update the scope of testing to accommodate the expanded list of disorders for which testing is done, update definitions, optimal timing, specific details regarding specimen collection, follow-up requirements to accommodate practice and technology changes in newborn screening. In addition, Authority and Reference citations are updated.

## Benefits of the Proposed Regulation Changes

The benefits anticipated by the adoption of these regulations are the protection of public health and safety by expanding upon existing regulation provisions and the improvement of provisions for early detection, follow-up, and referrals for diagnosis and treatment. This early detection will lead to early treatment, preventing illness, disability, and even death to infants. These regulations will further detail responsibilities of parties involved in the newborn screening services, such as hospitals, physicians, and NBS contracted laboratories.

## Policy Statement Overview

The California NBS Program has expanded its testing panel three times since the current regulations were developed, from four (4) tests detecting 29 diverse disorders to eight (8) tests detecting 80 diverse disorders. (See attached list of Disorders Detectable

by NBS Program as of January 1, 2012.) The requirements for screening have changed because the new disorders are so diverse and require different standards and practices. These necessary changes are not reflected in the current California Newborn Screening regulations.

Newborn Screening, as it is practiced internationally, nationally, and in California is a dynamic specialized program, constantly changing to meet the most current medical standards and practices in the field. The last substantive changes to NBS regulations were made in the 1980's. NBS terminology, guidelines, lab technology, forms, screening practices, identification of diverse disorders, detecting diverse disorders, and neonatal care has changed over the last 20+ years. Newborns are at risk for complications of disease, intellectual and developmental disabilities, and death if requirements are not changed in regulations to reflect the evolution of newborn screening principles and guidelines identified in the last 20 years. Perinatal licensed health facilities'/hospitals' staff, out-of-hospital newborn screening providers, and birth attendants (physicians and midwives) need to have access to and knowledge about these changes in NBS Program requirements so the newborns/infants of the state can be protected from the serious consequences of undetected disorders.

## Background and History of the Newborn Screening Program

### Authority for the NBS Program

The California Department of Public Health Genetic Disease Screening Program, previously called the Genetic Disease Branch, administers a statewide NBS Program for specific treatable heritable disorders and is authorized under the Health and Safety Code sections 124975, 124977, 124980, 124985, 124990, 124995, 125000, 125001, 125005, 125025, 125030 and 125035. This legislation is implemented by regulations in California Code of Regulations, Title 17, Division 1, Chapter 4, Subchapter 9, Group 3, Articles 1, 2, and 3.

### Program Description and History

The NBS Program currently oversees the screening of all live births in California (approximately 500,000 annually). The screening detects disorders that have varying degrees of severity, and if identified early, can be treated before they cause serious health problems, or even death.

The NBS Program began screening in 1966 for phenylketonuria (PKU), added screening for galactosemia and primary congenital hyperthyroidism (PCH) in 1980, and sickle cell disease and other hemoglobinopathies in 1990. On July 11, 2005, the NBS Program was expanded again to include over 40 additional metabolic disorders and one endocrine disorder, congenital adrenal hyperplasia (CAH). In July of 2007, the NBS Program was expanded again to include testing for cystic fibrosis (CF) and biotinidase deficiency (BD). In August 2010, the NBS Program began a pilot screening for severe

combined immunodeficiency and in 2012 permanently added this disorder to the testing panel.

**Summary of Treatment for NBS Disorders**

Ongoing health care and close monitoring help all children identified with any of the newborn screening disorders stay as healthy as possible. In addition, each of the identified disorders requires further specific care.

- Treatment for metabolic disorders (organic acid disorders, fatty acid disorders, and amino acid disorders (e.g. phenylketonuria or PKU)) varies by the condition, but includes close monitoring of a person's health, early identification of crisis in the baby's condition, medication, dietary supplements, special diets to avoid specific types of food, and/or avoidance of fasting.

- Treatment for galactosemia requires the substitution of soy formula for breast milk and formula within the first days of birth in order to prevent early death.

- Treatment for the endocrine disorders, primary congenital hypothyroidism (PCH), and congenital adrenal hyperplasia (CAH) includes the early and ongoing administration of hormone medications and early identification of gender issues (CAH).

- Detection of sickle cell disease in newborns makes possible early entry into comprehensive care, which includes the initiation of penicillin prophylaxis and parent education (e.g. identification of early warning signs of crisis and preventive health measures), factors which have been shown to reduce morbidity and mortality.

- Early detection of thalassemia disorders allows for close monitoring for infections and anemia.

- Early detection and treatment for cystic fibrosis (CF) allows for normal growth and development, prevention and/or reduction of serious infection, improved quality of life, overall health, and reduction of mortality.

- Infants identified with severe combined immunodeficiency or SCID (also known as the "bubble boy disease") have little or no immunity to disease and need to be protected from infection by environmental viruses (including weakened viruses in vaccines) and bacteria until treatment with bone marrow transplant or other treatment modalities can occur.

**Newborn Screening Process**

Specimens collected from the newborn by staff in perinatal licensed health facilities/hospitals or by midwives outside of facilities/hospitals are sent for analysis to one of several private laboratories under contract to the Department. The Department

also holds contracts with Newborn Screening Area Service Centers (ASC) in health care institutions across the state to follow-up with providers when inadequate specimens (those unable to be tested by the labs for various reasons) or early specimens (those collected prior to 12 hours of age) are sent. Staff of the ASCs also notify physicians and consult on initial positive screening results. Newborns with positive screening results are reported immediately to the primary care physician or facility/hospital physician/neonatologist (as indicated on the CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH-4409-(11-12)) NBS-I (D). The ASC staff makes recommendations to physicians about consulting with specialists and possibly referring these newborns to specialty physicians or to California Children's Services (CCS) specialty centers for consultation, diagnosis, and/or treatment. Referrals to specialists are often necessary because the disorders in the screening program are rare and general pediatricians are not always familiar with the disorder or its treatment.

In addition to follow-up for the detected disorders, families of newborns who are found to have hemoglobin trait or cystic fibrosis carrier status are sent a letter with information regarding traits. In the letter, they are asked if they would like to speak with a counselor about the genetic implications of these findings on future pregnancies and offered these services free of charge.

The California NBS Program also develops and distributes informational/educational material about NBS and the disorders included in the screening program. These are developed for providers (facilities/hospitals, midwives, and physicians) and families and are translated in a variety of languages to accommodate the cultural diversity of the state.

Other activities funded and implemented by the California NBS Program include:

- **GeneHELP (Genetic Health Education Link with Providers)**
- **Maternal PKU Program (for women diagnosed with PKU and are child-bearing age)**
- **Phenylalanine (Phe) Monitoring Program (provides ongoing phenylalanine testing for those diagnosed with PKU)**
- **Sickle Cell Education and Counseling Program**
- **Sickle Cell Counselor Certification**

## ARTICLE 1. DEFINITIONS

(Definitions are purposely numbered to allow for future additions while retaining the definitions in alphabetical order)

(1) Adopt §6500.03:

**§6500.03. California Children's Services (CCS).**
This new definition is necessary to assure clarity when the term is used in §6506.8(a). The definition in these proposed regulations is the same definition used in the CCS Regulations, Title 22, Division 2, Subdivision 7, Chapter 1, §41410.

Authority and Reference citations are added. The citations include those that are cited in the CCS regulations §41410.

(2) Adopt §6500.05:

**§6500.05. Confirmatory Test.**
This new definition is necessary as this term is being added to the regulations to replace the term "Recall Test" (§6500.67).

"Recall" is a term no longer used in the California NBS program or in the national NBS community. "Confirmatory" is the preferred term because it is a more explanatory and broader term, applying to additional testing for all of the disorders in the program, both those screened historically and those added to the NBS in program expansions.

Authority and Reference citations are added.

(3) Adopt §6500.9:

**§6500.9. Early Specimen.**
This new definition is necessary to accommodate the new requirement for testing to be done on newborns over 12 hours of age. Any newborn screening specimen collected on a newborn before 12 hours of age is an "Early Specimen" and providers must collect another specimen after 12 hours of age. (See §6505(a) for explanation of requirement for collection of specimen over 12 hours of age.)

Authority and Reference citations are added.

(4) Adopt §6500.21:

**§6500.21. Infant.**
This new definition is necessary to accommodate the fact that screening for some of the expanded disorders can be detected beyond the newborn period (defined in §6500.35 as "less than 29 days"). Screening and identifying positive results after the newborn period allows physicians to diagnose disorders and provide treatment, preventing

neurological and other physical damage, to infants who may not show symptoms until later in life. Damage to the child has often already occurred once symptoms occur.

The definition of infant in these proposed regulations is consistent with the definition used in Health and Safety Code section 124116 for the California Department of Health Care Services Newborn and Infant Hearing Screening Program. (See §6505(b) and (c).)

Authority and Reference citations are added.

(5) Adopt §6500.33:

**§6500.33. Lost to Follow-Up.**
This new definition is necessary to accommodate the use of the term in the subsections added to §6506.6 [§6506.6(e)], §6506.8 [§6506.8(b)], and §6506.10 [§6506.10(b)].

Authority and Reference citations are added.

(6) Amend §6500.35:

**§6500.35. Newborn.**
Amendment of this definition is necessary to be consistent with the definition used in Health and Safety Code section 124116 for the California Department of Health Care Services Newborn and Infant Hearing Screening Program.

Authority and Reference citations are updated.

(7) Amend §6500.39:

**§6500.39. Newborn's Physician.**
Amendment of this definition is necessary to clarify who is responsible for the care of the infant, for collection of the newborn screening, and for care of the infant if the newborn screening is positive. The phrase, "after discharge from the hospital" is deleted. The definition is therefore expanded to specifically clarify and include the different physicians who may be primarily responsible for caring for the newborn in the perinatal licensed health facility/hospital's normal newborn nursery, neonatal intensive care unit, and/or the physician caring for the newborn after discharge from the facility/hospital. If the newborn is in the Neonatal Intensive Care Unit (NICU), a neonatologist will be responsible for the care until discharged from the NICU to the care of the primary care physician (pediatrician or family practice physician). Additionally, in some facility/hospital systems, care of all newborns may be the responsibility of one facility/hospital physician while they are in the institution, and then will be transferred to the care of the primary care physician upon discharge from the perinatal licensed health facility/hospital. Changes in the definition include all these different situations and the specific physicians caring for the infant at any given time.

Authority and Reference citations are updated.

(8) Adopt §6500.43:

**§6500.43. Newborn Screening.**
This new definition is necessary to clarify for the regulated public what is meant by the "screening" that is included in the NBS Program, because "newborn screening" is different from other laboratory testing done to diagnose a disorder.

Authority and Reference citations are added.

(9) Amend §6500.45:

**§6500.45. Newborn Screening Area Service Center.**
Amendment of this definition is necessary to clarify the role of the Area Service Center (ASC) for providers. The ASCs in various regions of California are the primary contact centers between newborn screening providers and the Department. They educate providers regarding requirements of newborn screening and consult with them when specimens are early, inadequate, or positive. The changes retain the intent of the current definition, but change the wording for clarification. The changes also add a more specific description of the roles and functions of the NBS Area Service Center staff, so that providers will know what to expect from the ASC staff and how to utilize them.

Authority and Reference citations are updated.

(10) Adopt §6500.50:

**§6500.50. Newborn Screening Specimen.**
This new definition is necessary because the newborn screening specimen is a dried blood sample collected on a special filter paper that must be purchased from the Department, is specific to screening and different from many other blood specimens collected on infants. The specimen for screening is taken by a "heel stick" from the newborn's foot and the blood obtained is dropped onto the filter paper and dried before sending to the laboratory. Other blood specimens taken from newborns for confirmatory or diagnostic testing may be venous blood taken from veins or from intravenous lines.

Authority and Reference citations are added.

(11) Adopt §6500.51:

**§6500.51. Newborn Screening Test.**
This new definition is necessary to define and clarify the purpose of the newborn screening test and to identify its purpose – to detect risk for certain genetic and

congenital disorders. The definition is consistent with the definition of Newborn Screening in §6500.43.

Authority and Reference citations are added.

(12) Adopt §6500.55:

**§6500.55. Out-of-Hospital Newborn Screening Providers.**
This new definition is necessary to define and clarify the term added to the text in §6505(c), §6506, and §6506.6.

Authority and Reference citations are added.

(13) Adopt §6500.58 to read:

**§6500.58. Perinatal Licensed Health Facility Staff.**
This new definition is necessary to clarify what is meant when the text refers to the staff of a perinatal licensed health facility/hospital. Since there are many levels of staff in a facility, including those who are not direct patient care providers, it specifies and narrows the definition of staff to those who are actually in the departments that collect the newborn screening specimen.

Authority and Reference citations are added.

(14) Repeal §6500.65:

**~~§6500.65. Recall Specimen.~~**
The deletion of this definition is necessary, as the term “recall” is a term no longer used in the California NBS Program or in the national newborn screening community. “Confirmatory” is the preferred term. It makes clear and explains the purpose of the test – to confirm a positive result and applies to the confirmatory testing for all disorders in the program, both those screened historically and those added to newborn screening in program expansions. The term “recall” has been replaced with the term “confirmatory” in the text.

(15) Repeal §6500.67:

**~~§6500.67. Recall Test.~~**
The deletion of this definition is necessary, as the term “recall” is a term no longer used in the California NBS Program or in the national newborn screening community. “Confirmatory” is the preferred term. It makes clear and explains the purpose of the test – to confirm a positive result and applies to the confirmatory testing for all disorders in the program, both those screened historically and those added to newborn screening in program expansions. The term “recall test” has been replaced with the term “confirmatory test” in the text.

(16) Adopt §6500.71:

**§6500.71. Screening Information System (SIS).**
This new definition is necessary as the proposed regulations require (in §6506) perinatal licensed health facility staff to access a system developed by the Department to determine if a specimen has been received in the Department for testing. The system is called the "Screening Information System (SIS)" and is referred to in several places in the text. Therefore, a new definition is needed to clarify and explain the system and its use.

The current regulations (§6506) require that perinatal health facility staff review the newborn's medical record 14 days after discharge from the facility to make sure the newborn screening result is present in the record. The proposed regulations require the perinatal health facility staff to access the Screening Information System within seven (7) days after birth to make sure that a specimen has been received by the Department for testing; because the verification of receipt of the specimen is occurring earlier in the process, newborns who have not been tested can be identified earlier and tested.

Authority and Reference citations are added.

(17) Adopt 6500.78:

**§6500.78. This Group.**
This new definition is necessary to clarify the term used in §6500.71, §6501, and §6501.5 of this new regulatory action and in §6500.19, §6500.28, §6500.31, §6500.46, §6500.70, §6502.1, §6504.4, §6504.6, §6506.12, §6507, §6707.2, §6507.7, and §6508 of the Newborn Screening Program regulations not included in this regulatory action.

Authority and Reference citations are added.

## ARTICLE 2. TESTING AND FOLLOW-UP PROGRAM REQUIREMENTS

(Definitions are purposely numbered to allow for future additions while retaining the definitions in alphabetical order)

(18) Amend §6501:

**§6501. Scope of Newborn Testing.**
Amendment of this definition is necessary for two primary reasons:

1. There are two exceptions to the statement "each newborn born in California shall be tested…" and these exceptions have never been stipulated in this section of the regulations. The two exceptions are in §6501.2 ("if a parent or legally appointed guardian objects to a test on the ground that it conflicts with his or her religious beliefs or practices") and §6502 ("The provisions of §6501 shall not

apply if the newborn has a condition almost certain to be fatal in the first 30 days of life.”). The additions of these two exceptions in this section clarify and make this section more accurate. The proposed regulations therefore adds the phrase, “Except for provisions in §6501.2 and §6502” and changes the case of the word “each.”

2. The specific disorders screened for in the NBS Program change and expand based on national guidelines and California legislation. This section is revised to include the new disorders on the newborn screening testing panel that were authorized in the three program expansions of 2005, 2007, and 2012. These new disorders are outlined in Health and Safety Code sections 124977, 124980 and 125001 and are therefore not listed by name in these proposed regulations. In the event of future expansions, any new disorders can also be listed in these specified Health and Safety Code sections, which will mean future expansions will automatically be covered by the existing regulations and the regulations will therefore not have to be revised each time the program expands.

Authority and Reference citations are updated.

(19) Adopt §6501.5:

**<u>§6501.5. Required Newborn Screening Forms.</u>**
This new section is necessary as it codifies the requirement that newborn screening providers must obtain and use the following specific forms printed by and available only from the Department for various circumstances in the NBS Program and incorporates these forms by reference into the regulations. These forms include:

1. CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH–4409-(11-12)) NBS-I (D). (This form includes the special filter paper card used for the newborn screening specimen collection and a form which includes fields for demographic and clinical information used to identify the newborn and process the specimen. It also contains instructions for collecting an adequate NBS specimen. It is sent to and processed by a newborn screening laboratory.)

2. NEWBORN SCREENING TEST REFUSAL (NBS-TR) CDPH 4459 (06/11) – English version or CDPH 4459 (SP) (06/11) – Spanish version. (This form reports a refusal by the parent or legal guardian to have a newborn screened. This lets the Department know that the newborn’s test was not just missed, but that the newborn was not tested for this reason.)

3. HOSPITAL REPORT OF NEWBORN SCREENING SPECIMEN NOT OBTAINED (NBS–NO) CDPH 4089 (01/11). (This form reports to the Department that a screening specimen has not been obtained prior to the

newborn's discharge from the hospital. This initiates action by the designated ASC to locate and obtain a newborn screening specimen from the newborn.

4. NOTIFICATION OF REGISTRATION OF BIRTH WHICH OCCURRED OUT OF A LICENSED HEALTH FACILITY (NBS-OH) CDPH 4460 (01/09). (This form reports a birth registration of a newborn who was not born in a perinatal licensed health facility. The form is completed by the birth registrar when a parent or legal guardian registers the birth with the county. This initiates action by the designated ASC to check the Department database to determine if a newborn specimen has been obtained and if not, to locate and obtain a newborn screening specimen from the newborn.)

It is critical that the specific Department forms be completed and used so that all the necessary information for each circumstance can be transmitted to and processed by the Department.

Current regulations refer to the forms in various sections throughout the regulations and use vague language to describe the reporting to the Department. This section clarifies the utilization of the forms, makes the use of the forms specific and incorporates them by reference into regulation.

This change to the proposed regulations describes the NBS Program forms that providers must use. The new language defines the use of the forms and refers to the sections where the forms and their uses are described. The NBS Program added all the forms into this one section to make it easier to update the regulations in the future, and incorporate new forms by reference when they are revised and/or updated.

Authority and Reference citations are added.

(20) Amend §6505:

**<u>§6505. Collection of Newborn Screening Specimens.</u>**
Amendment of this section is necessary to update the newborn screening regulatory requirements to accommodate program expansions, new timing requirements for specimen collection, addition of the specific forms required by the Department and in order to ensure that providers understand and follow the new requirements. This ensures that infants are screened in a timely manner, diagnosed and treated promptly when positive screening results are found. The current §6505 has been deleted and has been completely revised. The subsections have also been "re-numbered" and "re-designated."

The changes eliminate old language that has been in existence in the NBS Program for 20+ years and replace this with current requirements based on the addition of the new, medically diverse disorders, as well as the technology and medical practice changes in newborn screening. It also provides more consistent time-frames regarding the

requirements for specimen collection in all circumstances. This section clarifies the updated requirements for collection of newborn screening specimens.

Subsections (a) through (d) specify actions required in the following different circumstances which can occur when a newborn is born:

(a) For newborns born in a perinatal licensed health facility:

This subsection is necessary to clarify the responsibility for collection of the newborn screening specimen when a newborn is born in a perinatal licensed health facility/hospital. There is often confusion when the newborn is born in one facility and transferred to another, this will help eliminate confusion by defining the responsibility for specimen collection by the birth facility/hospital.

Paragraph (1): The proposed language is necessary to clarify and specify the following:

- The specific form to be used for specimen collection, CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH-4409-(11-12)) NBS-I (D), referring the reader completing the form to the section in the regulations where the form is described and incorporated by reference - §6501.5(a) and to §6504.4(b) which describes the requirements for completion of the form and placement of the form in the newborn's medical record.

- The time-frame in which the specimen must be collected is between 12 hours and 96 hours of age. The collection after 12 hours of age is important as the baby's immaturity and physiological instability before this time does not give valid test results for some disorders (metabolic) on the testing panel. In addition, many analytes used to identify the newly added metabolic disorders do not begin to increase until after 12 hours of age and won't be detected in a specimen collected prior to 12 hours of age. Some newborns tested before that time will show negative results on the screening, when in fact they would be positive if tested after 12 hours of age. The language identifies any specimen collected under 12 hours of age as an "Early Specimen" and clarifies that another specimen must be collected after the newborn has reached 12 hours of age as outlined in §6506.6. It also reduces the "outside" time for collection of the specimen from 6 days, as outlined in the current NBS regulations, to 4 days (96 hours), thus facilitating collection, testing, and initiation of treatment as early as possible to avoid complications, morbidity and mortality.

- The exception to the rule for specimen collection by the birth facility is if the newborn is unstable or in a life-threatening condition. The priority in this circumstance is not the newborn screening, but the stabilization of the newborn's condition. If the newborn is unstable and transferred, as sometimes happens when they are born in a community perinatal licensed health facility/hospital and transferred to a facility with a specialized neonatal intensive care unit (NICU),

then the receiving facility/hospital must collect the specimen when the newborn is stable. The requirements for the receiving facility/hospital to collect the specimen within the appropriate time-frame, using the required form, and collecting a specimen prior to a transfusion are also outlined in the language.

Paragraph (2): The proposed language is necessary to clarify and specify the requirement that a specimen must be collected on any infant prior to a red blood cell transfusion, even if under 12 hours of age. The collection of a pre-transfusion specimen has always been a requirement of the NBS Program, because the transfusion of red blood cells will invalidate the test results for some of the disorders (hemoglobinopathies and galactosemia). So, the first specimen collected prior to the transfusion will be accurate for these disorders, and the second specimen, collected after transfusion will be accurate for the remaining disorders. The collection of specimens prior to 12 hours of age further complicates the collection. Testing for some metabolic disorders does not give accurate results in newborns under 12 hours of age, if the newborn is under 12 hours when a transfusion is needed, then another specimen must be collected after all transfusions have been discontinued. (See discussion of early specimens in §6505(a)(1).)

Paragraph (3): The proposed language is necessary to specify the requirement that the specimen must be given to a carrier for transport to the lab by the next business day of the designated carrier. This prevents the issue of “batching” (collection and holding specimens in the facility for several days so they can all be sent together in one mailing) which may result in degradation of specimens. NBS specimens held in warm temperatures or held too long may result in the laboratory not being able to test the specimen and they will be declared to be “inadequate.” In those cases, another specimen must be obtained. The language also specifies that transportation and handling of the specimen must be done by a carrier contracted with the Department or a contracted with a newborn screening laboratory. The Department may also designate the United States Postal Service (USPS) or another overnight courier as a carrier when the location of the specimen is a location that only the USPS or the designated overnight courier serves. This facilitates receipt of the specimens at the laboratory for testing within several days after collection. This also allows the reporting of any positives as soon as possible, and helps contain costs of transport. Other than the specific mention of the USPS, the carriers for transport are not named, as the Department requires the flexibility to contract with carriers that meet the highest standards at a reasonable cost for transport.

Paragraph (4): The proposed language is necessary to clarify the additional responsibility of the birth facility to complete the HOSPITAL REPORT OF NEWBORN SCREENING SPECIMEN NOT OBTAINED (NBS–NO) CDPH 4089 (01/11) to notify the Department that the specimen was not obtained for any reason. It specifies that the copy of the CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH-4409-(11-12)) NBS-I (D) should be present in the medical record providing evidence that a newborn screening specimen was collected, and if not found, the staff

must complete the HOSPITAL REPORT OF NEWBORN SCREENING SPECIMEN NOT OBTAINED (NBS–NO) CDPH 4089 (01/11). It also refers the reader completing the form to the section in the regulations where the form is described and incorporated by reference - §6501.5(c). Completion of this form notifies the Department about the birth and transfer. The regional Area Service Center will then track and assure that a specimen is collected by the receiving facility/hospital as soon as possible.

Paragraph (5): The proposed language is necessary to provide for the exception to collection of the newborn screening specimen in Subsection (a) if the parent or legal guardian objects to the screen; and the language describes the form to be completed to notify the Department.

(b) For newborns not born in a perinatal licensed health facility, but admitted to a perinatal licensed health facility at any time after birth:

This subsection is necessary to clarify the role of the perinatal licensed health facility for specimen collection when infants are NOT born in a perinatal licensed health facility, but are admitted to a facility at some time after birth. This language utilizes the newly-defined term, “infant,” to expand screening to children in these circumstances up to the age of one year, where applicable. This requirement helps assure that newborns born out of a perinatal licensed health facility, who may not have been screened (for any reason) will have a specimen collected, unless evidence of screening can be found.

Paragraph (1): The proposed language is necessary to clarify and specify the following:

- That the perinatal licensed health facility staff admitting an infant who was not born in a licensed health facility must quickly identify whether a NBS specimen has been collected and, if not, must collect a specimen within 48 hours of admission. This requirement assures that the specimen is collected, transported, and tested as soon as possible to detect any disorders in the infant. If disorders are detected, treatment can then begin to prevent health problems or death.

- The use of the Department’s required form for collection, CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH 4409-(05/11)) NBS-I (D). It also clarifies that all specimens shall be collected pursuant to two other sections in the regulations, §6501.5(a), which specifies the use of the CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH-4409-(11-12)) NBS-I (D) and §6504.4(b) which describes the requirements for completion of the form and placement of the form in the newborn’s medical record. Describing these other sections of the regulations here makes it easier for the staff to complete the forms so that testing is not delayed due to incomplete information.

- Review of the infant’s medical record for evidence of a previous specimen collection. The language further clarifies and directs them to collect a specimen

"unless a copy of the CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH-4409-(11-12)) NBS-I (D) or a copy of the NEWBORN SCREENING TEST REFUSAL (NBS-TR) CDPH 4459 (06/11), or a newborn screening result is found." If a NEWBORN SCREENING TEST REFUSAL (NBS-TR) CDPH 4459 (06/11) is found in the record, then the staff knows that the family has refused testing and no more discussion with the physician or family is required. If that form is not found and there is also no CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH-4409-(11-12)) NBS-I (D), then the staff must collect a specimen within 48 hours of admission to facilitate early detection of disorders.

- Checking to see if these forms are present in the record prevents collecting an additional specimen from the newborn if a specimen has already been collected and sent to the Department.

Paragraph (2): The proposed language is necessary to clarify the requirement that a specimen must be collected on any infant prior to a red blood cell transfusion, even if under 12 hours of age. The collection of a pre-transfusion specimen has always been a requirement of the NBS Program, because the transfusion of red blood cells will invalidate the test results for some of the disorders (hemoglobinopathies and galactosemia). So, the first specimen collected prior to the transfusion will be accurate for these disorders, and the second specimen, collected after transfusion will be accurate for the remaining disorders. The collection of specimens prior to 12 hours of age further complicates the collection. Testing for some metabolic disorders does not give accurate results in newborns under 12 hours of age, if the newborn is under 12 hours when a transfusion is needed, then another specimen must be collected after all transfusions have been discontinued. (See discussion of early specimens in §6505(a)(1) of ISOR.)

Paragraph (3): The proposed language is necessary to specify the requirement that the specimen must be given to a carrier for transport to the lab within 24 hours of collection. This time-frame prevents the issue of "batching" and potential degradation of specimens as described earlier. (See discussion of batching in §6505(a), Paragraph 3 of ISOR.) The language also specifies that transportation and handling of the specimen must be done by a carrier contracted with the Department or contracted with a newborn screening laboratory. The Department may also designate the United States Postal Service (USPS) or another overnight courier as a carrier if the location of the specimen is a location which only the USPS or other overnight courier serves. This facilitates receipt of the specimens at the laboratory for testing within several days after collection. This also facilitates the reporting of any positives as soon as possible, and helps contain costs of transport. Other than the specific mention of the USPS, the carriers for transport are not named, as the Department requires the flexibility to contract with carriers that meet the highest standards at a reasonable cost for transport.

Paragraph (4): The proposed language is necessary to clarify the additional responsibility of the perinatal licensed health facility to complete the HOSPITAL REPORT OF NEWBORN SCREENING SPECIMEN NOT OBTAINED (NBS-NO) CDPH 4089 (01/11) to notify the Department that the specimen was not obtained. It refers the reader completing the form to the section in the regulations where the form is described and incorporated by reference in §6501.5(c). Completion of this form notifies the Department about the birth and admission. The regional Area Service Center will then track and assure that a specimen is collected as soon as possible.

(c) For infants not born in a perinatal licensed health facility and not admitted to a perinatal licensed health facility after birth:

This subsection is necessary to clarify responsibility for specimen collection in the situation of a baby's birth that is not attended by a birth attendant, and is not subsequently admitted to a perinatal licensed health facility/hospital, but is seen in an "office" or clinic by a physician or other out-of-hospital newborn screening providers. This language utilizes the newly-defined term, "infant," to expand screening to children in these circumstances up to the age of one year, where applicable.

Paragraph (1): The proposed language is necessary to clarify and specify the following:

- That the infant must be screened within 48 hours of first contact with the physician to assure timely collection, testing, and treatment, if necessary.

- The use of the Department's required form for collection, CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH-4409-(11-12)) NBS-I (D). It also clarifies that all specimens shall be collected pursuant to two other sections in the regulations; §6501.5(a), which specifies the use of the CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH-4409-(11-12)) NBS-I (D) and §6504.4(b) which describes the requirements for completion of the form and placement of the form in the newborn's medical record.

- The responsibility to check the newborn's medical record for evidence of a prior screening or evidence that the parent/legal guardian refused screening. This prevents a duplicate screening being collected or the notification of a parent/legal guardian who has already refused screening.

Paragraph (2): The proposed language is necessary to stipulate the transportation of the specimen by a carrier contracted with and/or designated by the Department, so that the Department can specify and hold the carrier to agreed delivery schedules in contracts. (See §6505(a), Paragraph 3 of ISOR.)

Again, this subsection assures that infants, who may have been missed and not screened, will be identified and tested when seen in an outpatient setting. The

language specifies the time period within which the infant must be screened after being seen and also the time limit for transmitting the specimen to the lab for testing. This requirement helps assure that infants born out of a perinatal licensed health facility/hospital who may not have been screened (for any reason) will have a specimen collected, unless evidence of collection of a prior newborn screening or a newborn screening result can be found.

(d) For infants born outside of a perinatal licensed health facility and not subsequently admitted to a perinatal licensed health facility, and when the birth is being registered at the county registrar's office:

This subsection is necessary to clarify the role of the birth registrar to report the registration of the birth to the Department using the required form issued by the Department, NOTIFICATION OF REGISTRATION OF BIRTH WHICH OCCURRED OUT OF A LICENSED HEALTH FACILITY (NBS-OH) CDPH 4460 (01/09). The language refers the registrar to §6501.5(d) where the form is described and incorporated by reference. Upon receiving the notification of the birth, the Department can follow-up and determine if the infant has been screened, and if not, can arrange for collection of a specimen as soon as possible. It also specifies the time-frame within which the registrar must report the birth to the Department. The birth must be reported "the next business day after the birth is registered." This language applies to those births that are not delivered in a perinatal licensed health facility/hospital and are not subsequently admitted to a perinatal licensed health facility/hospital, but are being registered by the county registrar's office.

Subsection (e) codifies the option of screening a child over the age of one year if the physician deems such screening to be necessary:

This subsection is necessary to allow for circumstances that occasionally occur in which a child over the age of one year moves to California from another state, another country, or through other circumstances (e.g. adoption, etc.) and there is no evidence that a newborn screening has been done at any time since birth. The Department, in consultation with the baby's physician, may determine that the child would benefit from a newborn screening and can approve and arrange for the collection and testing of a specimen, even if the child is over one year of age. It is important for the Department to know that the child is over one year of age because the reference ranges and cut-offs for screening positives on some tests may need to be adjusted to accommodate that fact.

(f)~~(j)~~ The proposed re-designation of this subsection is necessary for consistency with the re-organization of §6505. The last phrase in the subsection is deleted as the Program has no statutory authority for its inclusion.

Authority and Reference citations are updated.

(21) Amend §6506:

**§6506. ~~Medical Record Review~~Verification of Receipt of Newborn Screening Specimens by the Department.**

Amendment of this section is necessary because the requirement for perinatal licensed health facility staff to check the medical record of the newborn fourteen (14) days after discharge, codified in the current regulations, has been changed to verification of receipt of a newborn screening specimen within seven (7) days of birth in the proposed regulations. In addition, the Department has added the requirement that out-of-hospital newborn screening providers (see new definition in §6500.55 of regulations text and ISOR) also check SIS to verify that specimens have been received by the Department. This is necessary to capture the additional specimens which should have been collected outside of a perinatal licensed health facility.

The title of the section is changed to reflect the change in the content of the section. The current §6506 has been deleted and the section has been revised. The changes eliminate old language that has been in existence in the NBS Program for 20+ years and replace it with current requirements based on the addition of the new disorders, as well as the technology and medical practice changes in newborn screening.

(a) The requirement for reviewing the medical record to assure the verification of receipt of newborn screening results has been an important part of the NBS Program. This has been the final “check” to assure that all infants have been screened. With the addition of the new disorders, the time it takes the Department to test the specimen in the laboratory has been increased. Therefore, the time for the results to be sent to the facilities has also increased. This is due to different testing methodologies and algorithms used for the new disorders. If the Department waited to have the perinatal licensed health facility staff or out-of-hospital newborn screening providers review the medical record for results to find out if an infant’s specimen was not received by the testing laboratory, the infant may already be affected by a disorder, resulting in morbidity and possibly death. As a result, the Department has developed a system that allows the facilities/hospitals to access and check a database that includes a listing of specimens received by the Department laboratories for testing. This necessitated the inclusion of a new definition for Screening Information System (SIS) in §6500.71 – and the requirement for perinatal licensed facility staff and out-of-hospital newborn screening providers to check that database within 7 days of birth to verify that a specimen has been received for all newborns at their facility. It specifies the copies of the forms that they should look for in the medical record, CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH-4409-(11-12)) NBS-I (D) to verify whether a specimen has been collected or not, and NEWBORN SCREENING TEST REFUSAL (NBS-TR) CDPH 4459 (06/11) – English version or CDPH 4459 (SP) (06/11) – Spanish version to determine whether the parents have refused testing.
If they find no verification of receipt of the specimen in the database, the language also specifies the actions they should take to report the missing specimen (the staff must enter a missing specimen report into SIS) and/or collect a specimen, if necessary.

Again, this assures the timely and prompt follow-up by the Department to collect specimens on infants who may have been initially missed.

The following sentence has also been added: "This applies to all infants for whom perinatal licensed health facilities and out-of-hospital newborn screening providers have responsibility for newborn screening pursuant to §6505(a), (b) and (c)." This addition is necessary to clarify that the perinatal licensed health facilities should check the database for all newborns/infants that have been born in their facilities (§6505(a)), or transferred or admitted to their facilities (§6505(b)), and that out-of-hospital newborn screening providers check the database for all newborns/infants in their care. This will ensure that they have verified that a screening has been collected for all newborns/infants in their care for whom they are responsible for collecting a screening.

(b) The new language in this subsection is necessary to allow perinatal licensed health facilities or groups of perinatal licensed health facilities to utilize their own systems to verify that specimens have been collected and received in the lab. These systems must meet the same criteria as the state system (as described in §6500.71(a) and (b) of regulations text), in order for them to be used for this purpose. Meeting the same criteria assures the quality of their system and the use of their system eliminates duplication of effort which would occur if they had to review the Department's Screening Information System as well as their own systems.

Authority and Reference citations are updated.

(22) Amend §6506.6:

**§6506.6. Follow-Up to Reports of Inadequate and Early Newborn Screening Specimens.**

Amendment of this section is necessary to include specifics and clarification of the follow-up of early specimens as the term "Early Specimen" and the requirement to collect specimens after 12 hours of age is new in these proposed regulations. (The use of the term "Inadequate Specimens" is already defined and used in current regulations.) The proposed change in this section deletes the current section in its entirety and proposes new language as follows:

The title and contents of this section are expanded to include not only the follow-up of inadequate specimens (those that the laboratory are unable to test for a variety of reasons, e.g. layered blood, not enough blood, etc.), but also the addition of the follow-up for those specimens collected "early" (on newborns less than 12 hours of age). The title of the section is changed to include the addition of "Newborn Screening" to clarify the specimen that is discussed in the section and differentiate it from other specimens collected on the infant (e.g. confirmatory or diagnostic) and the addition of an "s" to the word "specimen."

(a) This subsection is necessary to describe and clarify the process used by the Department when it receives a specimen believed to be “early” based on the information that is written on the CALIFORNIA NEWBORN SCREENING TEST REQUEST FORM (NBS-TRF) (CDPH-4409-(11-12)) NBS-I (D). The information on the form must be verified with the staff at the facility or out-of-hospital newborn screening provider which sent it to the Department, and then, if verified as early, another specimen must be sent as described in subsection (b).

(b) This subsection is necessary to clarify that the perinatal licensed health facility staff, birth attendant, out-of-hospital newborn screening provider, or newborn’s physician must collect another specimen within 48 hours of notification if an early specimen is sent to the Department. This assures that they act quickly to have the infant screened. It also reflects the urgency of testing and obtaining results, so treatment can be started if needed. The language also adds and clarifies the requirements for the timely collection and transmittal of an additional specimen to the Department for testing. The proposed language is necessary to specify the requirement that the specimen must be given to a carrier for transport to the lab by the next business day of the designated carrier. This prevents “batching” and degradation of specimens, as described earlier. (See §6505(a), Paragraph 3 of ISOR.) The language also specifies that transportation and handling of the specimen must be done by a carrier contracted with the Department or contracted with a newborn screening laboratory. The Department may also designate the United States Postal Service (USPS) or another overnight courier as a carrier. This allows the Department to maintain standards of timely transport, assuring that specimens arrive as soon as possible at the laboratory for testing. This also allows the reporting of any positives as soon as possible, and helps contain costs of transport. Other than the specific mention of the USPS, the carriers for transport are not named, as the Department requires the flexibility to contract with carriers that meet the highest standards at a reasonable cost for transport.

(c) This subsection is necessary to clarify the time-frames for action and the responsibility of the perinatal licensed health facility staff, birth attendant or newborn’s physician collecting another specimen if an inadequate specimen is sent to the Department. It specifies and shortens the time-frame within which the physician must act to either obtain another specimen or notify the Area Service Center that they were unable to do so from “within five days” to “48 hours” of notification. This assures that the physician acts quickly and in a timely manner to have the infant screened and reflects the urgency of testing and obtaining results, so treatment can be started if needed. The language also adds and clarifies the requirements for the timely collection and transmittal of an additional adequate specimen to the Department for testing. It specifies that the specimen must be given to a carrier for transport to the lab by the next business day of the designated carrier. This prevents “batching” and degradation of specimens, as described earlier. (See §6505(a), Paragraph 3 of ISOR.) The language also specifies that transportation and handling of the specimen must be done by a carrier contracted with the Department or contracted with a newborn screening laboratory. The Department may also designate the United States Postal Service

(USPS) or another overnight courier as a carrier if these entities are the only ones servicing a specific location. This facilitates receipt of the specimens at the laboratory for testing within several days after collection. This also allows the reporting of any positives as soon as possible, and helps contain costs of transport. Other than the specific mention of the USPS, the carriers for transport are not named, as the Department requires the flexibility to contract with carriers that meet the highest standards at a reasonable cost for transport.

(d) This subsection is necessary to clarify and specify that the perinatal licensed health facility staff, birth attendant, out-of-hospital newborn screening provider, or newborn's physician must act quickly (the language is changed from "as soon as possible" in the current language to "within 48 hours" in the proposed language) to notify the Area Service Center that they are unable to obtain another specimen when requested for either an inadequate or early specimen. The change also updates the method of notification to include newer technology available, such as fax and e-mail in addition to telephone.

The proposed language also removes the requirement in the current regulation language that the newborn's physician document details of the notification in their medical record (e.g. "Such telephone notification shall be noted in the newborn's physician's records specifying the date of notification, the person notified and the information provided"). The person from the Department (or Area Service Center) who speaks with the physician documents that information in the Department's Newborn Screening record. It is also difficult, if not impossible to monitor whether the physician has documented in the infant's medical record.

In addition, the last subsection (§6506.6(e)) is added to limit the newborn's physician's responsibility and liability to search for the infant if the infant is declared to be "Lost to Follow-Up" by the Newborn Screening Area Service Center.

Authority and Reference citations are updated.

(23) Amend §6506.8:

**§6506.8. Follow-Up to Reports of ~~Initial~~ Positive Results.**
Amendment of this section is necessary to specify the requirements for newborn's physicians when notified that a newborn screening test shows a positive result. The term "Initial" has been deleted in the title and in the text, as the process described is appropriate for positives on initial and also repeat specimens. The language, while it maintains the same time-frame required for physician action ("within 48 hours"), it specifies in subsection (a), the following two important requirements while still allowing flexibility and decision-making on the part of the newborn's physician:

(1) Consultation with a CCS specialist for the newborn's specific positive screening and possible referral to a CCS center based on the specialist's recommendation. This

requirement is important, especially for these specialized disorders that are often unfamiliar to and very rarely seen by general pediatricians. It assures that specialists who see these disorders more frequently and have specialized education and knowledge about treatment are consulted for their expertise. The NBS Program maintains a close association with CCS as it administers its protocols, guidelines, and regulations. It is important that physicians with infants of positive screenings consult with and possibly refer the families to CCS centers and/or CCS paneled physicians for diagnosis and treatment. As noted earlier, some of the disorders in the NBS testing panel are rarely seen by the general practice pediatrician or family care physician and may require complex diagnosis and treatment unfamiliar to them. The proposed language allows the general pediatrician/newborn's physician to maintain their professional relationship with the family and the newborn, while assuring that the best possible care is given to the newborn.

(2) Instruction to the newborn's family about any specific recommendations that need to be followed given the newborn's specific positive test. The newborn's physician can discuss these recommendations with the specialist, if he/she has questions about what to recommend.

In addition, the last subsection (§6506.8(b)) in the section is added to limit the newborn's physician's responsibility and liability to search for the infant if the infant is declared to be "Lost to Follow-Up" by the Newborn Screening Area Service Center.

This section also eliminates old language which is no longer appropriate for all the additional disorders screened for in the program. The term "recall" has been deleted and replaced with the term "confirmatory" to reflect current practice. (See Article 1. Definitions, §6500.05, §6500.65, and §6500.67 of ISOR.) It also utilizes the newly-defined term, "infant," to expand screening to children up to the age of one year, where applicable.

Authority and Reference citations are updated.

(24) Amend §6506.10:

**§6506.10. Use of Newborn Screening Contracted Laboratories for Repeat and ~~Recall~~Confirmatory Specimens ~~Collection and Transmittal~~.**

Amendment of this section, including its title, is necessary to reflect the use of laboratories contracted with the Department for confirmatory specimen testing. As the numbers and complexity of disorders has increased, the Department has contracted with labs for confirmatory testing of metabolic disorders screened using tandem mass spectrometry, galactosemia, cystic fibrosis, biotinidase, and severe combined immunodeficiency in order to assure quality control, rapid turn-around, and consistency with testing methodologies. As more disorders are added in the future, it is likely that additional confirmatory lab contracts will be added. In this updated language, the NBS Program requires the use of the contracted laboratories for confirmation of disorders. In

subsection (a), the proposed language specifies and clarifies the requirements for newborn's physicians to collect and send additional specimens in a timely manner and utilize appropriate containers for the specialized test to be performed (as some of these specimens need to be sent on ice or in containers that do not allow any light to enter the container, etc.). It also specifies that the physicians utilize Department-specified transmittal methods to ensure the timely delivery of the specimen, as well as requiring that they utilize the Department-contracted confirmatory laboratories for confirmatory testing when these contracts are in place.

It also not only requires newborn's physicians to utilize transportation of specimens as designated by the Department, but also provides flexibility for the Department to utilize appropriate and timely methods of transport for the specimens to the laboratory for testing. In the past, the United States Postal Service was generally used as the method of transport, but with additions of disorders that require quicker turn-around times, other companies that can provide one day or two day delivery service are being used (e.g. United Parcel Service, Golden State Overnight, etc.). As a result of shortened transit time, specimens can be tested; the diagnosis made; and affected infants treated sooner. As companies improve their ability to move specimens more quickly and contracts are renewed or changed for transportation of specimens, the timing and specifics of the days of service or days of business deliveries may change. These additions allow for changes in the contracts while not obligating the Department to a specific company, method of delivery, specific days and/or times for pick-ups and deliveries.

In addition, the last subsection (§6506.10(b)) is added to limit the newborn's physician's responsibility and liability to search for the infant if the infant is declared to be "Lost to Follow-Up" by the Newborn Screening Area Service Center.

This section also eliminates old language which is no longer appropriate for all the additional disorders screened for in the program. The new language in this section is included for the following reasons:

- The language has been changed to reflect the elimination of the term, "recall" (see reasons for deletions in §6500.65 and §6500.67 of ISOR) and the addition of the term, "confirmatory (see reasons for adoption in §6500.05 of ISOR).

- The language also utilizes the newly-defined term, "infant," to expand screening to children up to the age of one year, where applicable.

Authority and Reference citations are updated.

## Statement of Determination

### Economic Impact Analysis

The Department has determined that the regulation would not significantly affect the following:

1. **The creation or elimination of jobs within the State of California.** The proposal may result in the creation of jobs but its extent cannot be estimated.

2. **The creation of new businesses or the elimination of existing businesses within the State of California.** The proposal may result in the creation of new businesses but its extent cannot be estimated. The proposal should not result in the elimination of any existing businesses.

3. **The expansion of businesses currently doing business within the State of California.** The proposal may result in the expansion of businesses currently doing business with the State of California but its extent cannot be estimated.

4. **The benefits of the regulation to the health and welfare of California residents, worker safety, and the state's environment.** The proposal will significantly increase the benefits to the health and welfare of newborns born in California as it outlines protocols for the timely collection of newborn screening specimens; prompt testing, diagnosis and treatment when disorders are found. The proposal would not significantly affect worker safety in the State of California. The proposal would not affect the state's environment.

### Documents Relied Upon

N/A

### Alternatives Considered

The Department must determine that no reasonable alternative considered by the Department or that has otherwise been identified and brought to the attention of the Department would be more effective in carrying out the purpose for which the action is proposed or would be as effective and less burdensome to affected private persons than the proposed action or would be more cost-effective to affected private persons and equally effective in implementing the statutory policy or other provision of law.

### Attachment

Disorders Detectable by NBS Program as of January 1, 2012.