

**SURVEY OF MORBIDITY AND MORTALITY
AMONG HIGH RISK PRETERM INFANTS
(GDB)**

***Eunice Kennedy Shriver* NICHD
Neonatal Research Network**

Manual of Operations

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Chapter 1 Objectives and Study Designs

1.1 Introduction

This manual gives detailed instructions for the **Survey of Morbidity and Mortality Among High Risk Preterm Infants**. It is meant to serve as a reference guide for study staff, including investigators, coordinators, technicians and data managers. This study is being conducted by the *Eunice Kennedy Shriver* NICHD Neonatal Research Network.

1.2 Survey of Morbidity and Mortality Among High Risk Preterm Infants

The purpose of this study is to provide a registry of baseline and outcome data for high risk preterm infants, based on data collected in a uniform manner from neonatal intensive care units (NICUs) at institutions participating in the *Eunice Kennedy Shriver* NICHD Neonatal Research Network. These data, although not representative of a regional sample, do represent a number of major tertiary care academic centers. Although centers serve varying populations, they exemplify the neonatal morbidity problems of the 1980s through the 2010s and into the next decade. These data will be used to characterize the infants admitted to the units, to examine the relationships between certain entry characteristics and outcome, to measure trends in incidence of various disease entities, and to provide the basis for hypothesis formulation for Network multi-center studies.

Baseline and outcome data will be collected on all liveborn infants who are 1) inborn and between 401 grams and 1000 grams inclusive birth weight and/or 2) inborn and between 20 0/7 to 28 6/7 weeks (<29 weeks) inclusive gestational age. Infants enrolled in a Network RCT or prospective observational study (inborn and transferred infants) may be included in the GDB dataset if requested by the study subcommittee and approved by the NRN Steering Committee. These may be otherwise premature and/or low birth weight infants outside the GDB gestational and birth weight criteria. In addition, infants who meet the above criteria with a heart rate at birth, who died in the delivery room will be included. These data will be obtained by review of the mothers' and babies' charts. The data forms (listed in **Appendix F**) for the survey have been named '**generic data forms**' in recognition of the fact that the information collected is of universal interest and not specific to a particular disease or treatment. They provide a descriptive summary of the babies' background, perinatal and neonatal experience. Baseline data will be obtained soon after admission to the NICU and the outcome data will be obtained at the time of death or discharge from the hospital, transfer or 120 days.

Chapter 2 Administration

2.1 Organizational Structure

The Survey of Morbidity and Mortality Among High Risk Preterm Infants is being conducted by the NICHD Neonatal Research Network. The NICHD Neonatal Research Network was established by the Center for Research for Mothers and Children in 1986 to conduct multi-center clinical trials in neonatal medicine and management. The Network is funded as a cooperative agreement between the Clinical Centers, the Data Coordinating Center (DCC) and the NICHD. The Steering Committee for the Network is limited to the Principal Investigator from each Clinical Center, the Data Coordinating Center, and the NICHD Neonatal Research Program Official. Non-voting Steering Committee participants include the Director of the Center for Developmental Biology & Perinatal Medicine (CDBPM) and the Steering Committee Chairman, who is appointed by NICHD. The Steering Committee has the responsibility to develop study protocols and monitor their implementation.

2.1.1 Participating Centers

2.1.1.1 Clinical Centers

The Principal Investigators representing the Clinical Centers have agreed to abide by the study protocols and, in addition, to have comparable staff, facilities, and equipment. To ensure that centers meet standards for procedures, equipment and staffing, each center is certified prior to participation in Network studies.

2.1.1.2 Data Coordinating Center

The Data Coordinating Center (DCC) collaborates with the Steering Committee on protocol design, data management, data collection systems (including the final versions of protocols, forms and manual of operations), and analysis. The DCC conducts the interim and final statistical analyses and collaborates with the Steering Committee members in the preparation of publications based on the study results. The Principal Investigator of the DCC reports to the Steering Committee and the Data Monitoring and Safety Committee.

2.1.2 NICHD

In addition to its role as the funding agency, the NICHD participates as a voting member of the Steering Committee (the Program Official). NICHD staff also participates in the development of protocols and in assisting the Steering Committee in the coordination and publication of the studies conducted by the Network.

2.2 Committees

2.2.1 Steering Committee

This committee is comprised of the Principal Investigators from each of the Clinical Centers and the Data Coordinating Center, the NICHD Program Official, and the Chairman of the Steering Committee. The Steering Committee has the responsibility for identifying topics for network studies, designing study protocols, monitoring study implementation, and recruitment. The Steering Committee will also make recommendations for changes to study protocols if it deems

necessary. This committee receives recommendations from the Data Monitoring and Safety Committee via NICHD.

2.2.2 Generic Database Subcommittee

The Generic Database Subcommittee is responsible for the design of the generic data forms and for monitoring the conduct of the study. This subcommittee reports to the Steering Committee.

2.2.3 Publication Committee

The Publication Committee is responsible for developing the publication policy for the NICHD Neonatal Research Network and for writing the policy for the use of the Generic Data Base for publication.

Chapter 3

Survey of Morbidity and Mortality - Enrollment and Baseline Data

3.1 Enrollment

3.1.1 Eligibility

All infants who are 1) inborn and between 401 grams and 1000 grams inclusive birth weight and/or 2) inborn and between 20 0/7 to 28 6/7 weeks (<29 weeks) inclusive gestational age are eligible for the study. Infants enrolled in a Network RCT or prospective observational study (inborn and transferred infants) may be included in the GDB dataset if requested by the study subcommittee and approved by the NRN Steering Committee. These may be otherwise premature and/or low birth weight infants outside the GDB gestational and birth weight criteria. In addition, all inborn, liveborn infants who meet the above criteria and die prior to admission to the NICU are enrolled posthumously.

3.1.2 Screening Log Entry - Form NG01

The purpose of the Screening Log is to record all eligible infants admitted to all network centers. It serves as a cross check for identification and ensures that no infants are omitted for data collection. This form will not be entered into the center-based computer system. All infants should be entered on this log regardless if consent is required for GDB data collection.

3.1.2.1 NICU Admissions

For every infant admitted to the NICU who meet the above eligibility criteria, the Network Coordinator enters daily onto the log the baby's name, hospital record number, date of birth, birth weight, gestational age, if consent is obtained (if required at center) and whether or not enrolled in a NRN study.

The Network Number is each patient's unique identifier made up of a five digit Family Number (assigned to the pregnancy) plus the Birth Order Number. The Family Number is a consecutive number assigned (computer generated) when the infant is entered in the data management system (DMS). A Birth Order Number is assigned by the coordinator for all infants; for singleton or first born of a multiple birth, the code will be '1', each additional infant of a multiple birth will be assigned '2', '3', etc. If all infants of a multiple birth are not eligible for GDB, assign birth order number(s) starting with '1' for those infants who meet entry criteria.

This log may be modified to meet the particular needs of individual centers.

3.1.2.2 Deaths Prior to NICU Admission

The Network Coordinator will create a system to identify liveborn infants in the weight and gestational age range who expired prior to NICU admission. This is Center dependent and may be from weekly review of delivery room records, monthly reports from Morbidity & Mortality committees, etc. Name, hospital record number, date of birth, birth weight (measurement from the delivery room record), and Network number (as above) will be recorded on the screening log.

3.1.3 Data Forms

If the baby meets GDB eligibility criteria, forms NG02, NG03 and NG07 should be obtained and placed in a file folder designated for that baby. If the infant dies in 12 hours or less then replace

the NG03 with the NG03E and do not enter an NG07. Headers on all forms should be completed including Center number, Site number, infant's Network Number and mother's initials (optional)

Date and time format:

Date is mm\dd\yyyy unless otherwise specified

Time is recorded as 24 hour clock, day begins at midnight, 00:00.

3.1.4 Assignment of Network Number by Computer

The infant's identifying information should be entered into the DMS as soon as possible. This is known as the 'base' screen in the DMS and corresponds to the NG01 Screening Log.

The following information is contained on the NG01 and components of the base record:

Header Information

- **Center**
Two digit number for each NRN center, assigned by the DCC.
- **Site**
The NRN center assigns these to their hospitals that comprise the NRN center. Any site letter or number is acceptable. The site letter/number must be unique within the NRN center, consistent and never change even when a hospital is no longer part of the NRN center.

Data not keyed into the DMS

- **Infant's Name**
Last name followed by first name.
- **Infant's Hospital Number**
Two digit number for a center, assigned by the DCC.
- **GDB Consent**
Whether or not consent was obtained, if required.

Data keyed into the DMS

- **Date of Birth**
- **Birth Weight**
Record in grams.
- **Gestational Age**
Record the best estimate of gestational age, in weeks and days, using the following hierarchy:
 - Best OB estimate: Obstetrical measures based on last menstrual period, obstetrical parameters, and/or early (first trimester) prenatal ultrasound as recorded in the maternal chart.
 - Best Neonatologist estimate: Neonatologist's estimate based on physical criteria, neurologic examination, combined physical and gestational age exam (Ballard or Dubowitz), or examination of the lens. In instances when the gestational age in days is not recorded, enter '0' in the days field.

If the OB date based on last menstrual period (not early ultrasound) disagrees with the Neonatologist's estimate by more than 2 weeks, the Neonatologist's estimate should prevail.

Network

In the web-based EDC, the Network ID must be 6 digits long consisting of a 5 digit family ID (used to link siblings together from a multiple birth) and a 1 digit birth order number. The Network ID must begin with a value of 1 through 9, for example values of 100221 and 310002 are acceptable NETWORK IDs. The increased length of the NETWORK ID will ensure there are no duplicate IDs across the history of the GDB data collection and will quickly identify that the patient was keyed into the web-based EDC rather than the MS Access system.

Birth Number Assignment: for a single birth or first born of a multiple birth enter '1'.

For the second born code '2' etc. It does not necessarily have to conform to strict birth order from a multiple birth, but must be kept consistent for each baby. If any infant(s) of a multiple birth is not eligible for GDB, assign birth order number(s) starting with '1' for only those infants who meet entry criteria.

Users may use the EDC to automatically generate the Network ID or they may create it themselves. To automatically generate the Network ID click on the "Auto Generate Family Number" link found immediately below Q. 4 "Family Number" on the NG01 electronic case report form (eCRF). The system will populate a five digit family ID. The user will then key the birth number and the system will combine the two values and populate the Network ID in Q. 6 "Network" on the screen. Please record this ID on your paper case report forms.

To create the Network ID yourself simply key a unique family ID in Q. 4 "Family Number", enter the birth number and the EDC will combine the two values and populate the Network ID in Q. 6.

- **Infant enrolled in an NRN study**

For infants outside of the GDB gestational age and birthweight criteria

Infants enrolled in a Network RCT or prospective observational study (inborn and transferred infants) may be included in the GDB dataset if requested by the study subcommittee and approved by the NRN Steering Committee.

To identify these infants as correctly included on the NG01 "Enrolled in NRN Study" will be marked as "Y."

All GDB infants who meet usual GDB criteria do not require this documentation.

It is important to enter a 'base' screen for an infant as soon as possible, since at the time of entering data on the 'base' screen that infant is assigned a Network Number. This number is the infant's unique identifying number and should be used for all subsequent data forms.

When keying test data into the Data Management System (DMS), the user access mode should be set to "Training" (please review the DMS User's Manual for specific instructions). The DMS assigns a number starting with a 'T', such as 'T0001' to test records. When entering real data, the system will request the first 4 to 5 digits of the patient ID (dependent on the current size of your patient IDs), referred to as the Family ID. It then requests the patient's birth order number from the user. Lastly, the DMS creates the patient's NETWORK ID by combining the two

numbers together. For example, Network ID 688751 is made up of the family ID, 68875, and the birth order number, 1. The Network number can be up to 6 digits long.

3.1.5 Adding Network Numbers to NG01: Screening Log after Base Record Completion

After the base record is entered, enter the network number on the screening log and all of the infant's generic forms.

3.2 Baseline Data Collection

When a baby has been enrolled in this study, the coordinator should complete form NG02 with baseline information. Coding instructions are presented below. Most of the information required is standard in nature, and is to be obtained from the baby's chart and from the mother's medical record.

3.2.1 For Infants Participating in Clinical Trials

Masked Clinical Trials

For any question which asks if the infant received a medication with a 'Y/N' response, a code 'T' will be used when an infant has received the medication under a **masked** study protocol in which the infant may or may not have received the drug (for example, a placebo-controlled trial).

If at another time during the hospitalization or at discharge the infant receives the known medication as part of clinical care, the response would be changed to 'Y'.

When a **date of exposure/first dose** is required for any medication question coded as "T" for trial, record the date the infant first received the study medication (active or placebo) under a masked protocol. If at another time during the hospitalization or at discharge the infant receives the known medication as part of clinical care, the date entry would be changed to the date of the known medication administration. A comment will be added to state the infant previously received the medication under a masked study protocol.

When the **number of courses received** is required for any medication question coded as "T" for Trial the total number of courses will be left blank. If at another time during the hospitalization or at discharge the infant receives the known medication as part of clinical care, the number of courses would be changed to the number of known courses received. A comment will be added to state the infant previously received the medication under a masked study protocol.

When the **type** is required for any medication question coded as "T" for Trial, record the type as 'Other' and add a comment detailing the medication used in the trial. If at another time during the hospitalization or at discharge the infant receives the known medication as part of clinical care, the type would be changed to the type of known medication received. A comment will be added to state the infant previously received the medication under a masked study protocol, and the drugs used in that masked study protocol should be detailed.

Unmasked Clinical Trials

For **unmasked** trials where known medications or treatment were received (i.e., head-to-head trial of two steroids), code 'Y' if the active medication or treatment was received.

When a **date of exposure/first dose** is required, record the date the infant receives the medication under an unmasked study protocol

When the **number of courses received** is required, record the total number of courses the infant completed under the unmasked study protocol.

When the **type** is required, record the type of medication the infant received under the unmasked study protocol.

NG02: GENERIC BASELINE FORM

3.2.2 Section A - MATERNAL INFORMATION

The following information is to be obtained primarily from the mother's chart or any other reliable source. If possible, collect information about the mother while she is still in the hospital. This is the biological (birth) mother at the time of this delivery. If this is a surrogate pregnancy, code the surrogate mother's information.

1. **Mother's age**

Record the age in completed years at the time of delivery

2. **Pregnancy history (include this pregnancy)**

a. **Gravidity**

The number of confirmed pregnancies, including this one

b. **Parity**

The number of pregnancies reaching 20 weeks and 0 days of gestation or beyond, regardless of the number of fetuses or outcomes (ACOG 2014), including this delivery. It is the number of pregnancies reaching viability, and not the number of fetuses delivered, that determines parity. Note that each infant of a multiple birth should be assigned the same parity, and parity is only increased with birth of the last fetus. For example, if twins were born and it was the first delivery, then the parity for each twin would be 1. The parity for any children resulting from the next birth (whether singleton or multiple) following these twins would be 2. Note also that parity increases regardless of whether the fetus is liveborn or stillborn, as long as the pregnancy has reached at least 20 weeks.

3. **Marital status**

Choose the appropriate marital status code.

Code as follows:

1 = Married - If mother is married, currently married but separated (including legal separations), or common law marriage

2 = Single - If mother is single, divorced or widowed

6 = Unknown - If marital status is unknown

4. **Highest level of education achieved by the biological Mother**

Code the highest level of education achieved by the biological (birth) mother at the time of this delivery. If this is a surrogate pregnancy, code the highest education level of the surrogate mother at the time of delivery. This information should be obtained from the mother's or infant's medical record or other reliable source.

Code as follows:

- 1 = 8th grade or less - if completed 8th grade or less
- 2 = 9th to 12th grade - if completed through 9th, 10th, 11th or 12th grade and high school diploma not received
- 3 = High School diploma - if a high school diploma or GED was received and one full year of college was not attended
- 4 = Trade or Technical School
- 5 = Partial college or Associate's degree - if at least one year of college was attended or an Associate's degree attained but a B.A. or B.S. was not received
- 6 = College degree - if a Bachelor's (B.S. or B.A.) was received but no higher degrees were obtained
- 7 = Graduate degree - for degrees completed higher than a Bachelor's degree
- 8 = Unknown

5. Mother's medical insurance

Code all types of medical insurance documented in the maternal medical record at the time of admission. This information may often be found on the admitting or face sheet in the hospital record.

Code as follows:

- 10 = Public Insurance - this may include Medicaid, Medicare, a state funded program, federally funded program, or insurance obtained through the Affordable Care Act
- 3 = Private - this is traditional insurance, managed care, etc. (include CHAMPUS, Tricare or any insurance that may be tied to work).
- 5 = Self-Pay/uninsured - if hospitalization is to be or has already been paid for by the mother or other responsible party
- 6 = Unknown
- 9 = Other

6. Mother's ethnic categories

Code the mother's ethnicity as follows:

- 1 = Hispanic or Latino - A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term, "Spanish origin," can be used in addition to "Hispanic or Latino".
- 2 = Not Hispanic or Latino - None above
- 3 = Unknown or Not Reported - A person not knowing or not reporting ethnicity

7. Mother's racial categories

Code the mother's race as follows:

- 1 = Black - A person having origins in any of the black racial groups of Africa. Terms such as "Haitian" or "Negro" can be used in addition to "Black or African American."

- 2 = White - A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.
- 3 = American Indian or Alaskan Native - A person having origins in any of the original peoples of North, Central, or South America, and who maintains tribal affiliation or community attachment.
- 4 = Asian - A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam. (Note: Individuals from the Philippine Islands have been recorded as Pacific Islanders in previous data collection strategies.)
- 5 = Native Hawaiian or Other Pacific Islander - A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
- 6 = More Than One Race - A person having origins in multiple racial designations.
- 7 = Unknown or Not Reported - A person not knowing or not reporting race

8. Mother's height

Record the mother's height in inches or centimeters. If unknown select the code 'PM' to indicate permanently missing.

9. Mother's weight prior to pregnancy or during the first trimester

Record the mother's weight prior to pregnancy or during the first trimester in pounds or kilograms. If recording the first trimester weight, record the earliest weight available from the first trimester. If unknown select the code 'PM' to indicate permanently missing.

10. Mother's weight at delivery

Record the mother's weight at delivery in pounds or kilograms. If unknown select the code 'PM' to indicate permanently missing.

3.3.3 Section B - PREGNANCY COMPLICATIONS

The following information is to be obtained primarily from the mother's chart or any other reliable source. Items 4a and 5a may be coded as Yes, No or Unknown. Code 'Y' if the item is listed as a problem in the maternal or infant record. Otherwise code 'Unk' or 'N'.

1. Multiple birth?

Code 'Y' if there was a multiple birth.

If YES,

Complete only if this pregnancy is a multiple gestation. Do not include early (< 14 weeks) fetal reductions.

a. Number of fetuses

Include all fetuses, live or stillborn.

2. Is there evidence of prenatal health care in this pregnancy?

Use the following codes:

'1 = No' if no prenatal visit was noted.

'2 = Limited' if less than 3 visits or prenatal care started in third trimester.

'3 =Adequate' if greater than or equal to 3 visits and prenatal care started prior to third trimester.

3. Was fetal ultrasound dating obtained during pregnancy?

Code 'Y' if fetal ultrasound dating was obtained during pregnancy. Code 'N' if fetal ultrasound dating was not obtained. Code 'Unk' if it is unknown whether fetal ultrasound dating was obtained during pregnancy.

If YES, answer question 3.a. or 3.b. but not both:

a. Gestational age determined from first ultrasound:

Record the gestational age at the time of the first ultrasound as it was determined from first ultrasound in weeks and days. If the value for weeks is known and the value for days is unknown, record the data for days as missing (i.e., code "PM" or "**") rather than '0'.

b. If gestational age at ultrasound unknown, was ultrasound obtained during the first trimester?

Code 'Y' if ultrasound was obtained during the first trimester (<14 weeks' gestation). Code 'N' if there was no ultrasound obtained during the first trimester. Code 'Unk' if it is not known whether an ultrasound was obtained during the first trimester.

4. Diabetes prior to pregnancy?

Code 'Y' if diabetes mellitus was diagnosed prior to present pregnancy. Otherwise Code 'N'.

a. If YES, Type of diabetes?

Code:

'1 =Type 1' if Type 1 diabetes is documented. Type 1 diabetes is considered insulin deficient diabetes/ body does not produce insulin.

'2 =Type 2' if Type 2 diabetes is documented. Type 2 diabetes is considered insulin resistant diabetes/ body does not use insulin properly.

'3 =Unknown' if diabetes but type not documented.

b. If YES, Treatment(s) given

If multiple treatments used during the pregnancy, record the highest level using the following hierarchy:

1 = Insulin

2 = Oral hypoglycemic medication' if any oral hypoglycemic medication has been given.

See Appendix K for list of oral hypoglycemics

3 = Diet only

5 = None if no medication is given

6 = Unknown if type of medication given is not known.

5. Gestational diabetes (diagnosed during the pregnancy)?

Code 'Y' if gestational diabetes was diagnosed during the pregnancy.

a. If YES, Treatment(s) given

If multiple treatments used during the pregnancy, record the highest level using the following hierarchy:

Code:

1 = Insulin

2 = Oral hypoglycemic medication' if any oral hypoglycemic medication has been given.

See Appendix K for list of oral hypoglycemics

3 = Diet only

5 = None if no medication is given

6 = Unknown if type of medication given is not known.

6. Hypertension?

Code 'Y' if hypertension, chronic or pregnancy induced, is specifically recorded in the mother's chart. The standard definition of hypertension (maternal BP above 140 systolic or 90 diastolic) was recorded prior to or during the present pregnancy on at least 2 occasions.

If YES,

a. Hypertension existed prior to pregnancy?

Code 'Y' if patient had hypertension prior to this pregnancy documented in the chart and/or chronic hypertension.

7. Antepartum hemorrhage?

Code 'Y' if placenta previa, abruption or threatened abortion resulting in bleeding, which can be external (vaginal bleeding) or occult (retroplacental clot), is documented after 20 weeks of pregnancy. This does NOT include bloody show.

8. Was chorioamnionitis documented in the mother's medical record?

Code 'Y' if chorioamnionitis is specifically documented in the mother's medical record.

9. Was placental pathology performed?

If YES,

a. Was histologic chorioamnionitis documented?

See **Appendix Ia** for definitions.

b. Was acute funisitis documented?

Code 'Y' if acute funisitis is documented. Otherwise, code 'N'.

3.3.4 Section C - LABOR AND DELIVERY

1. Date and time of maternal hospital admission for this delivery:

a. Date:

From labor and delivery sheet, admission notes or other reliable source

b. Time:

From labor and delivery sheet, admission notes, or other reliable source. Use a 24

hour clock with midnight coded as 00:00. If time of admission is not specifically recorded in records, please use time of first maternal vitals.

2. **Was there rupture of membranes (ROM) prior to delivery?**

Code 'Y' if the time of rupture of membranes (ROM) was documented prior to the delivery. Note: If ROM at the same time as delivery, this question should be answered 'N'. For C-sections, if the date and time is not recorded, assume the time of ROM was at delivery and answer 'N'. Code 'Unk' if ROM is not documented.

If YES,

a. **Date:**

From labor and delivery sheet, admission notes or other reliable source

b. **Time:**

From labor and delivery sheet, admission notes, or other reliable source. Use a 24 hour clock with midnight coded as 00:00

c. **If date and/or time unknown, was ROM estimated at >18 hours?**

3. **Were antenatal steroids given to accelerate fetal maturity?**

Code 'Y' if corticosteroids (e.g. betamethasone, dexamethasone) were given during this pregnancy. Code 'N' if no steroids were given or 'Unk' if not documented.

a. **If YES, type of antenatal steroids given:**

Code the type of corticosteroid given, or both as documented in the maternal medical record. Code

- 1 = betamethasone
- 2 = dexamethasone
- 3 = both
- 4 = If unknown

If the mother is in a study and is receiving either the placebo or the drug, then answer 'T' to any questions concerning mother being on the drug.

b. **Was a complete course of antenatal steroids given?**

Code 'Y' if 2 doses of betamethasone or 4 doses of dexamethasone were given, as part of a single course, specifically to promote fetal maturation, with at least 24 hours from the first dose elapsed before delivery. If the time elapsed was less, this indicates that there was insufficient time for the drug to have an effect and would be considered incomplete. Information may be obtained from the maternal and/or infant chart. Count only doses that occurred prior to delivery. Code 'Unk' if unknown.

c. **Was more than one course of antenatal steroids given?**

Code 'Y' if any dose(s) beyond one complete course of antenatal steroids was given. Code 'N' if one or fewer courses of antenatal steroids were given. Code 'Unk' if the number of courses of antenatal steroids given is not known.

d. **When was the last dose of antenatal steroids given?**

i. **Date:**

Record the date on which last dose of antenatal steroids was given (day begins at 00:00, ends at 23:59).

ii. **Time:**

Use a 24-hour clock with midnight coded as 00:00.

4. **Were maternal antibiotics given within 72 hours prior to birth?**
Code 'Y' if any maternal antibiotics were used within 72 hours prior to birth.
 - a. **If YES, list antibiotics given**
Refer to **Appendix B**
5. **Was magnesium sulfate given during this admission prior to delivery?**
Code 'Y' if mother received magnesium sulfate during the admission prior to this delivery. Code 'N' if the mother did not receive it. Code 'Unknown' for incomplete records or if documentation is unclear.
6. **Was there documentation of electronic fetal heart rate monitoring within 12 hours prior to birth?**
Code 'Y' if there is documentation of continuous or intermittent electronic fetal heart rate monitoring within 12 hours prior to birth. Do not include monitoring with stethoscope or sonograms. Code 'N' if there was no electronic fetal heart rate monitoring within 12 hours prior to birth. Code 'Unknown' for incomplete records or if documentation is unclear.
7. **Final mode of delivery:**
As documented on labor/delivery sheet. Code:
 - 1 = Vaginal vertex
 - 2 = Vaginal breech
 - 3 = Cesarean section
 - 5 = Unknown or not noted in chart.

3.3.5 Section D - NEONATAL INFORMATION

1. **Date and time of birth:**
 - a. **Date:**
Record the date on which child was born (day begins at 00:00, ends at 23:59).
 - b. **Time:**
Use a 24-hour clock with midnight coded as 00:00.

NOTE: The day of birth is considered Day of life 1 even though it is not a complete 24 hour period. Day of life 2 is the next calendar day.
2. **Was the infant outborn?**
Code 'N' if the infant was born within the walls of one of the designated Network hospitals. Code 'Y' if the infant was born outside of the Network hospital. This could include any other hospital, home delivery, taxi, etc. This will include infants who are enrolled in an NRN trial who were not born at the Network center hospital.
If YES, date admitted to NICU
 - a. **Date admitted to NICU:**
Day begins at 00:00, ends at 23:59.
3. **Was a prenatal diagnosis made that influenced the decision to withdraw or limit intensive care?**
Code 'Y' if there was documentation in the mother's or infant's chart of a prenatal diagnosis other than immaturity or prematurity that has led to limitations of care. This may include, but is not limited to, withdrawal of life support, DNAR/DNR status or not

offering usual care such as respiratory support, nutrition, antibiotics, surgery or other diagnostic procedures.

- a. If YES, diagnosis (code all that apply),
Use Birth Defects Codes (**Appendix H**) to code a prenatal diagnosis made. If 'Other' diagnosis, specify. 'Other' codes include 199, 299, 399, 499, 599, 699 and 799, according to system involvement.
 - i. If OTHER, specify.

4. **Did the infant die ≤12 hours after birth?**

This includes infants who die in the delivery room.

IF YES, COMPLETE FORM NG03E.

5. **Sex:**

Code the stated sex of the infant.

1 = Male

2 = Female

3 = Ambiguous, there must be confirmation of ambiguous genitalia by either a genetics consult

at time of birth or pathology report if infant expires.

6. **Gestational age in weeks and days:**

Record the best estimate of gestational age.:

a. **Method used to determine recorded gestational age**

Code the method used to determine recorded gestational age.

1 = Obstetric estimate

Obstetric estimate is based on last menstrual period, obstetrical parameters, and/or early (first trimester) prenatal ultrasound as recorded in the maternal chart.

2 = Neonatal estimate

Neonatologist's estimate is based on physical criteria, neurologic examination, or combined physical and gestational age exam (Ballard, Dubowitz or Finnstrom).

If the OB date based on last menstrual period (not early ultrasound) disagrees with the Neonatologist's estimate by more than 2 weeks, the Neonatologist's estimate should prevail.

7. **Apgar score - 1 minute:**

Use the official one minute Apgar score as assigned in the delivery room from delivery chart.

8. **Apgar score - 5 minute:**

Use the official five minute Apgar score as assigned in the delivery room from delivery chart..

9. **Apgar score – 10 minutes**

Use the official 10 minute Apgar score as assigned in the delivery room from delivery chart.

10. Birth resuscitation/stabilization:

Code 'Y' for all support provided to the infant at the time of birth.

a. Oxygen?

Supplemental O₂ (FiO₂ > .21) delivered to the infant via face mask, hood, CPAP, or ET tube.

b. Positive pressure ventilation?

Positive pressure ventilation with face mask or prongs and using an anesthesia bag or devices such as Neopuff.

c. CPAP?

Continuous positive airway pressure delivered by CPAP device or mask.

d. Intubation?

Insertion of a tube (even if transiently) into the trachea to allow positive pressure ventilation for breathing. If intubation was done for suctioning or to give surfactant and immediately removed, it should not be included here.

e. Chest compression?

External pressure over central chest to contract the heart.

f. Epinephrine?

Epinephrine delivered intravenously or intratracheally for resuscitation.

11. Is there documentation of delayed cord clamping?

Code 'Y' if infant had documented delayed cord clamping. Otherwise code 'N.'

1. If YES, timing of cord clamping delay

Code the timing of cord clamping delay:

1 = < 30 seconds

2 = 30 – 60 seconds

3 = > 1 min – 3 min

4 = > 3 min – prior to stop of pulsation

5 = Until stop of pulsation

6 = Other, specify _____

12. Is there documentation of cord milking?

Code 'Y' if infant had documented cord milking. Otherwise code 'N.'

13. Birth weight:

Record the birth weight in grams of the infant as recorded in one of the following places on the chart in order of preference (an individual center may employ a different ordering if it is deemed more reliable):

- 1) On the labor and delivery record
- 2) On the nursery admission record
- 3) On the admission physical examination form
- 4) The pathology report when an infant expires

14. Length:

Record the length in centimeters, as recorded on the admission physical or in the child's medical record within 72 hours of birth.

15. Head circumference:

Record the head circumference in centimeters as recorded or in the child's medical record within 72 hours of birth:

- 1) On the admission physical exam form
- 2) On the nursery admission record
- 3) The pathology report if the infant died

16. Was any thermal product used to improve temperature regulation?

Code 'Y' if source documentation is found on thermal wrap use in the patients chart. Code "N" if there is no source documentation. At sites where thermal wrap use at delivery is "*standard of care*" but source documentation cannot be found, Coordinators should code this question with 'Unknown' to indicate unknown. Thermal wraps may include NeoWrap, saran wrap, any kind of polyethylene (plastic) wrap/bag, or exothermic mattress. Do not include plastic covers, warming bed or tents used to cover the infant in an open bed warmer while in the NICU.

17. Record infant's first temperature documented after admission to nursery?

Record the first temperature recorded following admission to the nursery. For centers who admit infants to a holding area or a delivery room stabilization area, record the first temperature taken in this location. Record the temperature in Centigrade or Fahrenheit.

b. Celsius

c. Fahrenheit

c. Date

d. Time

e. Source

Record the source of the temperature as:

- 1 = rectal
- 2 = axillary
- 3 = skin

Chapter 4 Survey of Morbidity and Mortality - Outcome Data Collection

4.1 Overview of Clinical Outcome Data Collection

Outcome data will be collected for each infant from time of birth until Status is reached. Detailed information is listed below.

4.2 Clinical Outcome - Forms NG03, NG03E and NG05

The outcome data form NG03 (to be completed from the baby's chart through day 120, discharge, transfer or death, whichever comes first) was designed to summarize each baby's clinical course. For infants who die in 12 hours or less, the early death form NG03E is completed in lieu of the NG03 and NG07, as there are many questions on the NG03 and NG07 which do not apply to infants who die early. In addition, because an infant's values for some items on NG03 could change after 120 days of hospitalization, form NG05 was created. The NG05 (late clinical outcome form) contains a subset of the items on NG03 and should be completed only for infants hospitalized greater than 120 days, after they have died, have been discharged or have been transferred.

It is very important that form NG03 or form NG03E be coded and entered in the DMS as soon as possible after the baby's discharge, transfer, death or as soon as possible after day 120. When applicable, paper documentation versus electronic should be obtained prior to the infant's chart leaving the NICU for Medical Records.

It should be noted that form NG03 or form NG03E should not be held back for coding or entry into the DMS by waiting for the autopsy report. If the autopsy result for cause of death is to be included and results are not yet available, enter the temporarily missing data code 'TM', and enter final autopsy cause of death in the DMS when it becomes available.

4.2.1 *Discharge from the NICU to Home*

This is the straightforward case: The first date the baby is discharged to home, the baby's clinical data are all obtainable from the medical record. If the baby is readmitted to the NICU from home, no further data will be collected.

4.2.2 *Transfer to Another Location within the Center*

When the baby is transferred from the NICU to a step down unit, another floor, or even another hospital within the same clinical center, the coordinator is still expected to keep track of the baby and complete form NG03 when the baby finally leaves the clinical center.

4.2.3 *Transfer to Another Facility*

The Network Coordinator should attempt to determine the final outcome (death or discharge) for each baby that is transferred out of the clinical center to another facility. If an infant is transferred back within 7 days (without being discharged to home), do not count this as a discharge but rather as a continuous admission.

Transfer to another NRN Center does not meet the NRN definition of transfer (status). The following procedures should be followed to document a transfer between NRN Centers and to allow for complete and accurate collection of GDB data for infants transferred from one NRN Center to another NRN Center during the hospitalization. Institutional and local IRB policy should be followed for the release and transfer of information between hospitals.

The procedures outlined below should be strongly considered when completing the hard copy paper forms for an infant that is transferred from one NRN Center to another. Completion of the electronic forms will depend on the individual case and the Centers involved.

The NRN Center of origin for the transferring infant will complete required GDB forms with the most current status of the infant for receiving NRN center.

NG02 will be the responsibility of the originating hospital, as this information is available from the maternal record and admission documents for the infant.

NG03E will not be included, as any infant born at an NRN center who dies within 12 hours of birth will not likely be a candidate for transfer.

For infants transferred ≤120 days of age, the following data forms should be provided by the transferring center to the receiving center:

NG03

Provide a Y response to any question where the infant has already 'met' the data point, even if it may occur again (i.e. sepsis or pneumothorax). Otherwise, leave question unanswered and this will be completed by the receiving center at discharge, death or 120 days per usual NRN practice.

Provide all responses, Y/N or dates for questions that are time limited if the infant has reached or surpassed the time point noted in the question. This would include questions that ask for data in the first 24 hours, <72 hours, first 28 days or at 36 weeks. If the infant has not reached the time point, leave blank.

Provide responses for questions even if the item may be ongoing (i.e. episode of sepsis, surgeries) or questions where the data may be updated after transfer (i.e. most severe cranial sonogram).

Provide all counts up to the time of transfer for questions that ask for number of days (i.e. breast milk) or number of courses (i.e. indomethacin/ibuprofen). Provide the end date of counts to allow the receiving center to continue the counting as needed.

NG07

Complete all time points the infant has reached for the cumulative number of days of each parameter (HFV, CV, Nasal ventilation, CPAP, NC, oxygen). Complete the highest mode of support for each of the time points met. For time points not yet met, leave blank and provide dates for each type of support the infant has received since the last time point met.

If an infant is transferred >120 days, the NG07 will have been completed by the transferring hospital.

For infants transferred >120 days of age, the following data forms should be provided by the originating center to the receiving center:

NG05

If the infant is >120 days of age and still hospitalized in the receiving NRN center, complete the data form starting with section B for questions that would be answered Y. If the infant has not had the problem (i.e. problem that has caused hospitalization >120 days or treatment, testing or ethics/palliative care) leave the questions blank.

4.2.4 *Death*

The cause of death is recorded using descriptions and codes listed in **Appendix C**.

4.3 **NG03: GENERIC CLINICAL OUTCOME FORM**

4.3.1 *Section A - STATUS*

1. **Status of infant at time of completion of form**

1 = if infant was discharged to home

2 = if infant is still in the hospital at 120 days

3 = if infant was transferred to another facility without returning to a Network hospital within 7 days. This includes transfers to hospitals outside the Network Center or chronic care facilities

5 = if the infant died

2. **Date of status**

Record date of status.

3. **Weight at status**

Weight in grams on day of status (preferably), or within 7 days.

4. **Length at status**

Length in centimeters on day of status (preferably), or within 7 days.

5. **Head circumference at status**

Head circumference in centimeters on day of status (preferably), or within 7 days.

4.3.2 *Section B - ETHICS/PALLIATIVE CARE*

1. **At any time after birth (prior to NG03 Status) was there documentation of discussion with parents to limit, withdraw or not escalate care?**

Code 'Y' if after 120 days, there was documentation of a discussion with parent to limit, withdraw or not escalate care. Otherwise, code 'N'.

2. **Were the following treatments withheld, limited or withdrawn at any time with the intent to limit care?**

Code 'Y' to all that apply, otherwise code 'N'.

a. **Intubation/ventilation**

b. **Nutrition/Hydration**

3. **Palliative care consult obtained?**

Code 'Y' if there was documentation that a palliative care consult was obtained. Otherwise code 'No'.

4. **Ethics consult obtained?**

Code 'Y' if there was documentation that an ethics consult was obtained. Otherwise code 'N.'

4.3.3 *Section C - TRANSFER*

This section refers to when the infant is sent to another hospital or chronic care facility without returning in 7 days. Complete this section if status (A1) of infant at time of completion of this form is "transferred."

1. **Date of transfer:**
Record date of transfer.
4. **Final outcome:**
 - 1 = if the baby died in hospital (informed via telephone contact or letter from the other hospital)
 - 2 = if the baby was discharged to home
 - 3 = if the baby remains in the hospital at one year of age

4.3.4 Section D - DISCHARGE ALIVE

Complete this section if the Status (A1) of the infant at the time of completion of this form is discharged home'

1. **Date of discharge to home**
Record date of discharge.
2. **Discharged home on continuous oxygen?**
Code 'Y' if discharged home on continuous oxygen. Code 'N' if otherwise'.
3. **Discharged home on any of the following medications?**
Code 'Y' if infant is discharged home on any medication(s) listed below. Code 'N' if otherwise. For questions 3.a.-3.i., code 'T' if infant discharged on a trial medication in a masked placebo controlled study. Refer to section 3.2.1 for details.
 - a. **Diuretics** - including but not limited to furosemide, spironolactone, chlorothiazide, or hydrochlorothiazide
 - b. **Bronchodilators** - including but not limited to albuterol
 - c. **Anticonvulsants** - including but not limited to phenobarbital, dilantin, valproic acid, depakane, carbamapazine
 - d. **Antireflux medications** - including but not limited to ranitidine, famotidine, metaclopramide.
 - e. **Antihypertensive medications** - including but not limited to hydrazaline.
 - f. **Methylxanthines** - including but not limited to caffeine, theophylline, and aminophylline.
 - g. **Inhaled steroids** - including but not limited to budesonide (pulmicort) and fluticasone (flovent).
 - h. **Systemic steroids** – including but not limited to dexamethasone, hydrocortisone, and prednisone/prednisolone.
 - i. **Other, specify**
Specify other medication on which infant was discharged home. Do not include multivitamins or iron.
4. **Discharged home receiving any human milk?**
Code 'Y' if infant is discharged home receiving any human milk. Code 'N' if otherwise.
 - a. **If YES, type of milk**
Use the following codes:

- 1= Maternal Milk
- 2= Donor Milk
- 3= Both
- 4= Unknown

4.3.5 Section E - DEATH

Complete this section if the Status of the infant at time of completion of this form is '5=Death' or if the final outcome for a transferred infant is 'Died in Hospital.' Include additional information about death that becomes available after status (such as blood culture results, late entered discharge notes, etc.)

1. **Date of death:**
Record date of death.
2. **Autopsy performed?**
Code "Y" if autopsy performed. If an autopsy is performed, the cause of death should not be coded until the results of the autopsy are known. Code 'N' otherwise.
3. **Contributory cause of death:**
This should be the underlying, proximate disease which initiated the series of events leading to death. This underlying cause must be (1) etiologically specific and (2) antecedent to all other causes with respect to time and pathologic relationship. Without the underlying cause, death would not have occurred. The cause of death should be based on both clinical evidence and autopsy findings. In the absence of an autopsy, the clinical evidence will be used. Only one option is coded after consultation with the PI or alternate PI.

A list of the causes of death are in **Appendix C**.
4. **If cause of death is code 10 (Congenital malformation), code 31 (Sepsis, specify organism), or code 90 (Other), specify.**

Part 2: 36 WEEK INFORMATION

4.3.6 Section F. –36 Week Information

If the infant has not been discharged by 36 weeks gestational age then record the following information at 36 weeks gestational age.

1. **Status at 36 weeks**
 - 1 = infant discharged to home
 - 2 = infant in the hospital at 36 weeks gestational age
 - 3 = infant transferred to another facility without returning in 7 days
 - 5 = infant died
- If "2," (In hospital)**
- a. **Date of 36 week measurement**
Record the actual date that this measurement was taken.

NOTE: The measurements may not be taken on the same calendar day, but all should be within the window at 36 weeks (± 7 days). If all the measurements are not taken on the same day, then the date recorded should be that of the weight at 36 weeks ± 7 days.

- b. **Weight**
Record the weight in grams at 36 weeks (± 7 days) gestational age
- c. **Length**
Record the length in centimeters at 36 weeks (± 7 days) gestational age
- d. **Head circumference**
Record the head circumference in centimeters at 36 weeks (± 7 days) gestational age

Part 3: Organ Systems

4.3.7 Section G - PULMONARY

1. **Did the baby receive surfactant?**

This includes any surfactant preparation used at any location (delivery room, NICU or at referring hospital).

If YES, record the following:

a. **Date of first dose?**

Record the date the first dose was given (day begins at 00:00, ends at 23:59).

b. **Was first dose given in the delivery room?**

Code 'Y' if first dose was given in the delivery room. Code 'N' otherwise.

c. **Type of surfactant given:**

Record the type of surfactant given:

1 = Beractant (Survanta)

2 = Poractant alfa (Curosurf)

3 = Calfactant (Infasurf)

9 = Other

d. **Was the surfactant mixed with budesonide?**

Code 'Y' if the surfactant administered was mixed with budesonide. Code 'N' if otherwise. Code 'T' if the infant was enrolled in the BiB trial. If 'TI' refer to section 3.2.1 for detailed instructions.

e. **Method of administration:**

Record the method of administration:

1 = ETT (endotracheal tube) – includes INSURE (INTubate, SURFactant, REMove) given using an endotracheal tube

2 = LISA/MIST (less invasive surfactant administration or minimally invasive surfactant treatment) – defined by use of a specialized catheter used to inject surfactant below the vocal cords

3 = Aerosolized – may be given using a nebulizer via mask or prongs

4 = LMA (laryngeal mask airway)

9 = Other

2. **Pneumothorax?**

Code 'Y' if pneumothorax is documented in the infant's chart. Pneumothorax is a collection of air in the pleural space where a lucency is identified in the pleural space with displacement of the lung away from the chest wall. Do not include a pneumothorax resulting from a thoracotomy during surgery (e.g. PDA ligation).

3. **PIE?**

Code 'Y' if pulmonary interstitial emphysema (PIE) is documented in the infant's chart. PIE is a radiographic and pathologic diagnosis made when air ruptures from alveoli or small airways into the perivascular tissues of the lung. This diagnosis will only be documented from the radiographic reports. Do not include PIE documented in the patient notes unless there is radiographic documentation to support this diagnosis. Otherwise code 'N'.

4. **Pulmonary hemorrhage?**

Code 'Y' if there was bright red blood per the ET tube associated with clinical deterioration.

5. **Steroids for BPD/CLD?**

Code 'Y' if the infant received any doses or courses of systemic steroids to prevent or treat bronchopulmonary dysplasia/chronic lung disease. Do not include inhaled steroids or doses of steroids given for extubation and/or stridor.

If initial treatment/medication is given under a masked or unmasked study protocol or if subsequent medication is received as part of clinical care post trial, refer to Section 3.2.1 for detailed instructions.

Code 'N' otherwise.

a. **If YES, Date of first dose:**

If 'Y' record the date the infant received the first dose of steroids or trial medication.

b. **Was more than one course given,?**

Code "Y" if more than one course was given. Code 'N' otherwise.

c. **Was total exposure > 14 days**

Code 'Y' if the total exposure was > 14 days. Code 'N' otherwise.

d. **Drugs prescribed**

Code the type of drugs prescribed.

2 = dexamethasone

6 = hydrocortisone

7 = prednisolone.

6. **Did infant receive inhaled nitric oxide?**

Code 'Y' if infant received inhaled nitric oxide.

If initial treatment/medication is given under a masked or unmasked study protocol, or if subsequent medication is received as part of clinical care post trial, refer to section 3.2.1 for detailed instructions.

a. **If YES or Trial, Date of first exposure**

If 'Y' or 'T', record the date of first exposure. If 'T' refer to section 3.2.1 for detailed instructions.

7. **Did the infant receive vitamin A?**

Code 'Y' if infant received vitamin A.

If the treatment/medication was given under a masked or unmasked study protocol, or if subsequent medication is received as part of clinical care post trial, refer to section 3.2.1 for detailed instructions.

4.3.8 Section H - CARDIOVASCULAR

1. **Patent ductus arteriosus (PDA)?**

Code 'Y' if clinical evidence of left to right PDA shunt documented by continuous murmur, hyperdynamic precordium, bounding pulses, wide pulse pressure, congestive heart failure, increased pulmonary vasculature or cardiomegaly by CXR, and/or increased oxygen requirement or ECHO evidence of PDA with documentation of left to right ductal shunting. Code 'N' if otherwise.

If YES, **Treatment**

a. **Indomethacin?**

Code 'Y' if infant received indomethacin. If infant treatment/medication was given under a masked or unmasked protocol, or if subsequent medication is received as part of clinical care post trial refer to section 3.2.1 for detailed instructions. Code 'N' otherwise.

b. **Ibuprofen?**

Code 'Y' if infant received ibuprofen. If infant treatment/medication was given under a masked or unmasked protocol or if subsequent medication is received as part of clinical care post trial refer to Section 3.2.1 for detailed instructions. Code 'N' if otherwise.

c. **Acetaminophen?**

Code 'Y' if infant received acetaminophen. If infant treatment/medication was given under a masked or unmasked protocol or if subsequent medication is received as part of clinical care post trial refer to Section 3.2.1 for detailed. Code 'N' if otherwise.

d. **Cardiac catheterization for PDA closure?**

Code 'Y' if the infant had a cardiac catheterization for PDA closure. Code 'N' if otherwise. Failed catheterization closures should also be included.

IF YES,

1. **Date of cardiac catheterization for PDA closure**

If 'Y' record the date the cardiac catheterization for PDA closure was performed.

2. **Was the cardiac catheterization for PDA closure successful?**

Code 'Y' if the cardiac catheterization for PDA closure was successful.
Code 'N' if otherwise.

e. **Surgery?**

Code 'Y' if surgical ligation was required to close the PDA. Code 'N' otherwise.

f. Other?

Code 'Y' if another treatment such as coils was used. Do not include fluid restriction.

If YES, specify treatment given. Code 'N' otherwise.

2. Was the infant treated for hypotension in the first 24 hrs of life?

Code 'Y' if the infant was treated for hypotension in first 24 hours of life. Code 'N' if otherwise.

If YES,,

a. Volume bolus?

Code 'Y' if a volume bolus was given. Code 'N' otherwise.

2. Initiation of vasopressors?

Code 'Y' if there was an initiation of vasopressors. Code 'N' otherwise.

3. Initiation of systemic steroid?

Code 'Y' if there was an initiation of systemic steroid. Code 'N' otherwise.

3. Was an echocardiogram done to monitor for pulmonary hypertension?

If YES,

a. Date

Record date of the echocardiogram done to monitor for pulmonary hypertension.

b. Results: Evidence of pulmonary hypertension?

Code:

1= Yes if there was evidence of pulmonary hypertension

2= No if there was no evidence of pulmonary hypertension.

3= Equivocal if the evidence was ambiguous or uncertain.

4.3.9 Section I - NEUROLOGY

1. Was indomethacin given within the first 24 hours of life?

If the infant was known to have received indomethacin within the first 24 hours of life, code as 'Y'. If infant was enrolled in a masked or unmasked protocol, or if subsequent medication is received as part of clinical care post trial, refer to Section 3.2.1 for detailed instructions. Code 'N' otherwise.

2. Were seizures confirmed by EEG?

Code 'Y' if there was documentation of EEG findings that were consistent with seizures. Code 'N' otherwise.

3. Were any cranial sonograms done within 28 days of birth?

Code 'Y' if cranial sonograms were done within the first 28 days of life. Code 'N' otherwise.

IF NO, GO TO QUESTION I6

- a. If YES, **Are all studies without evidence of intracranial hemorrhage, periventricular leukomalacia or ventriculomegaly?**

Intracranial hemorrhage refers to any bleed in the brain, including germinal matrix.

IF YES, GO TO QUESTION I6.

If No, continue with question I3b.

- b. **Date of sonogram with most severe findings:**

Record the date of the cranial sonogram with the most severe findings within the first 28 days. Determination of the most severe findings should be based on the following rank order from least severe to most severe. Least severe is blood/echodensity in the germinal matrix/subependymal area followed by blood echodensity in the ventricle, ventricular dilatation and blood/echodensity in the parenchyma is the most severe. **Use the earliest scan of an infant in whom multiple scans have the same most severe findings.**

For discrete lesions, echodensity or increased echogenicity may be considered equivalent.

PLEASE NOTE: Document all the findings on the cranial imaging identified above. For all imaging studies (questions I3, I7 and I8) only record definite findings and do not record those that are interpreted as uncertain, probable or possible. **If it is unclear how to record the results of an image, discuss findings with the PI or his designee.** The documentation for items 3c-3g does not correspond to a grade of hemorrhage. Items 3c-3g should be considered independent of each other and therefore an infant may have more than one item recorded. For items d-g, indicate side of involvement by coding 'Y' under right (R), left (L), or both. Questions about midline shifts are not right and left but yes and no answers.

- d. **Blood/echodensity in germinal matrix/subependymal area?**

Code 'Y' if blood/echodensity in the germinal matrix/subependymal area is documented. **When blood echodensity is seen in the ventricle but NOT in the germinal matrix, code 'N' for germinal matrix hemorrhage.**

- d. **Blood/echodensity in the ventricle?**

Code 'Y' if blood/echodensity in the ventricle is documented. This finding should be recorded independent of the size of the ventricle. Indicate side of involvement right, left or both.

- e. **Ventricular size enlarged with concurrent or prior blood in the ventricles?**

Code 'Y' if ventricular enlargement occurs in association with blood/echodensity in the ventricular system on any scan. Indicate side of involvement, right, left or both.

- f. **Ventricular size enlarged without concurrent or prior blood in the ventricles?**

Code 'Y' if ventricular enlargement occurs without blood/echodensity in the ventricular system on any scan. Indicate side of involvement, right, left or both.

- g. **Blood/echodensity in the parenchyma?**

Code 'Y' if blood/echodensity in the parenchyma is documented. Intraparenchymal echodensities may or may not be accompanied by blood/echodensity in the ventricle. Intraparenchymal echodensity differs from diffuse increased echogenicity. Indicate side of involvement, left, right or both.

NOTE: For sonographic reports that are limited to a grade of ICH (usually I-IV) without a description of the findings record as follows:

- Grade I: record 'Y' for question 3c
- Grade II: record 'Y' for question 3d
- Grade III: record 'Y' for questions 3d and 3e
- Grade IV: record 'Y' for question 3g

For sonographic reports that are limited to isolated ventricular dilatation without other associated findings (**no blood/echodensity in ventricles**) record 'Y' for question 3f. If YES,

1. **Midline shift.**

Code 'Y' if midline shift was documented. Code 'N' otherwise.

h. **Blood/echodensity in the basal ganglia or the thalamus?**

Code 'Y' if blood/echodensity in the basal ganglia or the thalamus is documented. Code 'N' otherwise.

i. **Cerebellar hemorrhage?**

Code 'Y' if cerebellar hemorrhage was documented on the cranial ultrasound. Code 'N' otherwise.

For sonographic reports that contain both a grade of ICH and a description, prioritize the descriptive findings over the assigned grade if the two pieces of information are not consistent. **Confirm the latter prioritization with the PI.**

4. **Cystic Periventricular Leukomalacia (cPVL) within 28 days?**

Record as cPVL when this diagnosis is used. In the absence of a diagnosis of cystic PVL on sonographic reports, use cPVL when cysts (echolucencies) are described in the white matter around the ventricle. These cysts are most commonly dorsal and lateral to the external angle of the lateral ventricle. Echolucencies may be single or multiple, may be bilateral or unilateral, may vary in size, and may be diffuse or focal in distribution along the front to back axis of the head. **If PVL is reported and cysts or echolucencies within the brain parenchyma are not specified, review the scan with the PI or designee of the PI to verify the presence of this finding.** Indicate side of involvement by coding 'Y' under right (R), left (L), or both. Code 'N' otherwise.

5. **Porencephalic cyst within 28 days?**

Porencephalic cyst will be used to lump all cystic disease other than cystic PVL. In the absence of a diagnosis on sonographic reports, use porencephalic cyst when there is a single unitary cyst within the cerebral hemisphere that may or may not communicate with the lateral ventricle. These cysts may be congenital and can be present on sonograms shortly after birth, or may evolve over time at the site of a previous parenchymal blood/echodensity (3g from above). These cysts may also be termed post-hemorrhagic cysts, or if multiple, multi-cystic encephalomalacia. Do not include subependymal cysts or choroid plexus cysts as part of this category. The latter two are minor cysts that will not be recorded. Indicate side of involvement by coding 'Y' under right , left , or both. Code 'N' otherwise.

6. **Were any cranial imaging studies done after day 28?**

Code 'Y' if any cranial imaging was done after day 28. Code 'N' otherwise.

If No, Go to Section J.

7. **Was a sonogram performed after day 28?**

Code 'Y' if sonogram was performed after day 28. Code 'N' if otherwise.

If YES, record information for the sonogram closest to 36 weeks postmenstrual age.

a. **Date of image**

Record the date of the imaging study closest to 36 weeks PMA.

b. **Normal Study?**

Code 'Y' if the results of the cranial imaging closest to 36 weeks postmenstrual age was reported to be normal.

If Yes, go to Question I8.

If No, go to Question I7c-e.

If NO,

c. **Ventricular size enlarged?**

Code 'Y' if ventricular size was documented to be enlarged. Indicate side of involvement if enlarged by marking 'Y' under right, left or both.

d. **Cystic Periventricular Leukomalacia (cPVL)?**

Record as cPVL when this diagnosis is used. In the absence of a diagnosis of cystic PVL on sonographic reports, use cPVL when cysts (echolucencies) are described in the white matter around the ventricle. These cysts are most commonly dorsal and lateral to the external angle of the lateral ventricle. Echolucencies may be single or multiple, may be bilateral or unilateral, may vary in size, and may be diffuse or focal in distribution along the front to back axis of the head. **If PVL is reported and cysts or echolucencies within the brain parenchyma are not specified, review the scan with the PI or designee of the PI to verify the presence of this finding.** Indicate side of involvement by marking 'Y' under right , left , or both.

e. **Porencephalic cyst?**

Porencephalic cyst will be used to lump all cystic disease other than cystic PVL. In the absence of a diagnosis on sonographic reports, use porencephalic cyst when there is a single unitary cyst within the cerebral hemisphere that may or may not communicate with the lateral ventricle. These cysts may be congenital and can be present on sonograms shortly after birth, or may evolve over time at the site of a previous parenchymal blood/echodensity (3g from above). These cysts may also be termed post-hemorrhagic cysts, or if more than one, multi-cystic encephalomalacia. Do not include subependymal cysts or choroid plexus cysts as part of this category. The latter two are minor cysts that will not be recorded. Indicate side of involvement by marking 'Y' under right , left , or both.

8. **Was an MRI performed after day 28?**

Code 'Y' if MRI was performed after day 28. Code 'N' if otherwise.

If YES , record information for the MRI closest to 36 weeks postmenstrual age.

- a. **Date of image:**
Record the date of the imaging study closest to 36 weeks PCA.
- b. **Normal Study?**
Code 'Y' if the results of the cranial imaging closest to 36 weeks postmenstrual age was reported to be normal.
If Yes, go to Section J.
If No, complete I8c-e.
- c. **Ventricular size enlarged?**
Code 'Y' if ventricular size was documented to be enlarged. Indicate side of involvement if enlarged. Indicate side of involvement by marking 'Y' under right , left , or both.
- d. **Cystic Periventricular Leukomalacia (cPVL)?**
Record as cPVL when this diagnosis is used. In the absence of this diagnosis, code cPVL when cysts are described in the white matter surrounding the ventricle. Cysts may be single or multiple, may be bilateral or unilateral, may vary in size, and may be diffuse or focal in distribution from the front to back (cephalad to caudad) axis of the head. Non-cystic PVL should not be recorded under this entry. Indicate side of involvement by marking 'Y' under right , left or both.
- e. **Porencephalic/posthemorrhagic cyst/multicystic encephalomalacia?**
Porencephalic cyst will be used to lump all cystic disease other than cystic PVL. Use porencephalic cyst when there is a single unitary cyst within the cerebral hemisphere that may or may not communicate with the lateral ventricle. These cysts may be congenital and be present on sonograms shortly after birth, or may evolve over time at the site of a previous parenchymal blood/echodensity (3g from above). These cysts may also be termed post-hemorrhagic cysts, or if multiple, multi-cystic encephalomalacia. Do not include subependymal cysts or choroid plexus cysts as part of this category. The latter two are minor cysts that will not be recorded. Indicate side of involvement by coding 'Y' under right , left , or both.

4.3.10 Section J - GASTROINTESTINAL

1. **Total days of parenteral nutrition?**
Record the number of days on which the baby received parenteral alimentation including amino acids or lipid solution at some point during the day. Enter '0' if baby never received parenteral nutrition of any type described above.
2. **Did the baby receive enteral feeds?**
Code 'Y' if the infant was fed enterally. Feeds consist of formula or breast milk. Colostrum priming is coded as enteral feeds. Sterile water is not considered enteral feeding. Code 'N' otherwise.

If YES,

- a. **Type of first enteral feeding?**
Code type of enteral feeds infant first received. If more than one type of feed is given record the type that made up the majority of the first feeding:

1 = Maternal milk

2 = Donor milk

3 = Formula

b. Date of first enteral feed

Record the date of the first enteral feed.

c. Did enteral feeds reach 120 ml/kg/day?

Code 'Y' if the enteral feeds reached 120 ml/kg/day. Calculate using the current weight. Code 'N' otherwise.

If YES,

3. Date first achieved?

Record the date first achieved.

d. Type of human milk infant received in the first 28 days?

Code all types of human milk received in the first 28 days:

1 = Maternal if the infant only received maternal milk in the first 28 days

2 = Donor of the infant only received donor milk in the first 28 days

4 = None if the infant did not receive maternal milk, donor milk or was not in a feeding trial in the first 28 days

e. Type of fortification of human milk

Code the type of fortification of human milk:

1 = bovine-based fortifier

2 = human milk-based fortifier

3 = Both

4 = Neither

f. Did the infant receive probiotics in the first 28 days?

Code 'Y' if the infant received probiotics in the first 28 days.

If infant treatment/medication was given under a masked or unmasked study protocol, or if subsequent medication is received as part of clinical care post trial, refer to Section 3.2.1. Code 'N' otherwise.

See Appendix L for list of probiotics.

3. Proven necrotizing enterocolitis (NEC) diagnosis

Code the correct response using the Modified Bell's Staging Criteria for NEC in **Appendix G**. Also refer to **Appendix I**.

0 = Absent/Suspect when there is no necrotizing enterocolitis present or Bell's Stage IA or IB.

2 = Proven, no surgery, Stages IIA, IIB or IIIA

- 3 = Proven, surgery, Stage IIIB
- 4 = Proven, autopsy

Code type of surgery to include laparotomy or drain and other procedures in Section Q using Appendix E.

a. If proven NEC, record date of first episode.

Record date of first episode. If proven NEC is discovered during the autopsy then list the date of death as the date of first episode of proven NEC.

b. Did the infant restart feeding after first episode of NEC?

Code 'Y'; if the infant restarted feeding after the first episode of NEC. Code 'N' otherwise.

If YES,

i. Date feeding restarted after first episode of NEC

Record date feeding restarted after first episode of NEC.

c. Was creatinine measured?

Code 'Y' if at least one serum creatinine was measured within 10 days of the diagnosis. Code 'N' otherwise.

If YES,

1. Highest value

Record highest serum creatinine level obtained in mg/dL.

2. Date

Record date highest serum creatinine level was measured.

4. Spontaneous gastrointestinal perforation without proven NEC?

Code 'Y' if the infant has a spontaneous gastrointestinal perforation without necrotizing enterocolitis. Code 'N' otherwise..

a. If YES, Date of the first spontaneous GI perforation

Record the date on which the first spontaneous gastrointestinal perforation occurred.

5. Did the infant receive any type of enema as therapy for meconium ileus or obstruction?

Code 'Y' if infant received any type of enema as therapy for meconium ileus or obstruction. Code 'N' otherwise.

a. If YES, date of the first enema

Record date of the first enema.

6. Did the infant have GI surgery that resulted in short gut?

Code 'Y' if the infant had surgery involving the GI tract that resulted in the diagnosis of short gut which includes malabsorption, severe diarrhea, gastric hypersecretion, secondary bacterial overgrowth and failure to thrive. Record surgical procedure in Section Q. Code 'N' otherwise.

4.3.11 Section K - HEARING

1. Was a hearing screen performed prior to status?

Code 'Y' if a hearing screen was performed to evaluate the infant's hearing prior to status. Code 'N' otherwise.

If YES,

a. Was otoacoustic emissions (OAE) testing performed?

Code 'Y' if OAE testing was performed. Code 'N' otherwise.

If YES,

1. Was OAE failed?

Code 'Y' if infant failed the OAE. Otherwise, code 'N'.

If YES,

i. Unilateral or bilateral fail?

Code

1=Unilateral

2=Bilateral

b. Was automated auditory brainstem response (AABR) performed?

Code 'Y' if automated auditory brainstem response (AABR) was performed.
Code 'N' otherwise.

If YES,

1. Was AABR failed?

Code 'Y' if infant failed the AABR. Otherwise, code 'N'.

If YES,

i. Unilateral or bilateral fail?

Code

1=Unilateral

2=Bilateral

2. Was a diagnostic auditory brainstem response (ABR) performed prior to status?

Code 'Y' if there was documentation of an ABR performed prior to status. Otherwise, code 'N'.

If YES,

a. Was hearing loss documented?

Code 'Y' if hearing loss was documented. Code 'N' if no hearing loss was documented.

If YES,

2. Unilateral or bilateral hearing loss?

Code
1=Unilateral
2=Bilateral

4.3.12. Section L - OPTHALMOLOGY

Appendix D contains a Retinopathy of Prematurity (ROP) Diagram.

1. Was an exam performed for Retinopathy of Prematurity (ROP)?

Review the medical record to determine if an examination was performed for ROP and flag all examinations found in order to answer the remainder of the questions. Code 'Y' if an ophthalmologist examined the infant's eyes for ROP. The examinations usually begin at 4 to 6 weeks and continue until the retinal vasculature is mature. If coded as 'N', no other questions in this section are required.

If YES,

a. Was ROP diagnosed in either eye?

Code 'Y' if ROP diagnosed prior to Status (any stage) in either eye in any of the examinations. Code 'N' otherwise.

If YES,

(1) Did ROP reach stage 3 or worse in either eye?

Code 'Y' if it reached stage 3 or worse in either eye. Code 'N' otherwise.

(2) Did plus disease develop in either eye?

Plus disease is noted by the ophthalmologist in addition to the stage and zone. It is recorded as present or not. Sometimes it is referred to as "posterior pole vascular dilation and tortuosity". Usually if this is present on any examination, it is close to the worst ROP examination for the infant. Code 'Y' if plus disease was observed on the worst examination recorded above for either eye. When the posterior veins of the retina are enlarged and the arterioles tortuous, then the designation "plus" is added to the ROP stage number. For example, Stage 2 with plus disease is sometimes written 2+. Code 'N' otherwise.

(3) Did infant have stage 1 or stage 2 ROP diagnosed in Zone 1?

Code 'Y' if infant had stage 1 or stage 2 ROP diagnosed in Zone 1. Code 'N' otherwise.

b. Intervention therapies:

(1) Was retinal ablation performed in either eye (laser and/or cryotherapy)?

If 'Y' code type and date of surgery in Section K using Appendix E. Code 'N' otherwise.

(2) Was scleral buckle or vitrectomy performed in either eye?

If 'Y' code type and date of surgery in Section K using Appendix E. Code 'N' otherwise.

(3) Avastin or other anti-VEGF drug

Code "Y" if the infant received Avastin or other anti-VEGF medication.

If infant treatment/medication was given under a masked or unmasked study protocol, or if subsequent medication is received as part of clinical care post trial, refer to Section 3.2.1. Code 'N' otherwise.

c. **At the time of reaching status, indicate the most appropriate description as described below:**

1 = Determined, favorable in both eyes

EACH eye met one of the following criteria

- Mature vessels (fully vascularized)
- Immature vessels in zone III for two consecutive examinations
- Acute ROP of stage 1 or 2 in zone III for two consecutive examinations
- ROP in zone II or zone III but determined to be clearly regressing

2 = Determined, severe ROP in either eye

Severe: EITHER eye met one of the following criteria

- Received surgery for ROP
- Retinal detachment from ROP
- Avastin injection or Anti-VEGF drug

3 = Undetermined ROP status in either eye (and neither had “severe ROP”)

Undetermined: EITHER eye met one of the following criteria, code reason under (1):

- 1 = Immature vessels in zone I or zone II
- 2 = Immature vessels reaching zone III for only 1 examination
- 3 = Stage 1 or 2 ROP in zone III for only 1 examination
- 4 = Stage 3 ROP in zone III
- 5 = ROP in zone I or zone II
- 6 = Plus disease

4.3.13 Section M - HEMATOLOGY

1. **Blood type of infant**

- 1 = A
- 2 = B
- 3 = AB
- 4 = O
- 5 = Unknown

a. **Rh (Rhesus) factor?**

Code

- 1 = Positive
- 2 = Negative
- 3 = Unknown

2. **Was the infant transfused with pRBC?**

Code 'Y' (if infant received packed red blood cells at any time prior to status. Code 'N' otherwise.

If YES,

a. Date of first pRBC transfusion

Record the date of the first pRBC transfusion.

b. Lowest hemoglobin OR hematocrit prior to first transfusion

Record either the lowest hemoglobin (g/dL) or hematocrit (%) prior to first transfusion.

Only one of these values needs to be entered. Use the one that is used most often for any clinical judgments at your center.

c. Total number of pRBC transfusions

Record the number of transfusions

3. Was the infant transfused with platelets?

If Yes, (complete M3a-b); If "No" (skip to M4)

a. Date of first platelet transfusion:

Record the date of the first platelet transfusion

b. Lowest platelet count before transfusion

Record the lowest platelet count

4. Did the infant receive erythropoietin or another erythropoiesis stimulating agent?

Code 'Yes' if infant received erythropoietin or another erythropoiesis stimulating agent.

i.e. Erythropoietin alfa (Procrit, Epogen). Darbepoietin alfa (Aranesp).

If initial treatment/medication is given under a masked or unmasked study protocol or if subsequent medication is received as part of clinical care post trial, refer to section 3.2.1 for detailed instructions. Code 'n' otherwise.

4.13.14 Section N – RENAL

1. Clinical Diagnosis of Acute Kidney Injury - AKI?

Code 'Y' if there is a clinical diagnosis of acute kidney injury (AKI) at any time during the NICU stay. Code 'N' otherwise.

If YES,

a. Date of diagnosis

Record date clinical diagnosis of AKI was made.

b. Inpatient consult with or referral to outpatient nephrology?

Code 'Y' if the clinical team either requested an inpatient pediatric nephrology consultation or made a referral for an outpatient evaluation by pediatric nephrology.

Code 'N' otherwise.

2. Blood Pressure at status?

Record blood pressure (systolic and diastolic) measured within ± 1 week of status status in mmHg

3. Was there a diagnosis of hypertension?

Code 'Y' if there was a diagnosis of hypertension. Code 'N' otherwise.

If YES,

a. Were antihypertensives used?

Code 'Y' if the infant was treated for hypertension with any of the following: amlodipine, captopril, enalapril, enalaprilat, hydralazine, isradipine, labetalol, Lisinopril, nicardipine, propranolol. Code 'No' otherwise.

b. Week #

Record days 1-4 in the first row and days 5-7 in the second row. In the next rows record the week number for week's 2-6.

c. Maximum creatinine date

Record the date the maximum serum creatinine was obtained for each timepoint.

1. Maximum creatinine value

Record the maximum serum creatinine value in mg/dL for each timepoint.

d. Minimum creatinine date

Record the date the minimum serum creatinine was obtained for each timepoint.

1. Minimum creatinine value

d1. Record the minimum serum creatinine value in mg/dL for each timepoint.

4.3.15 Section O - INFECTION

Organism codes for this section are listed in **Appendix A**. If the organism is not included in the list, code as '010' (to be assigned), and notify the DCC that a new code should be assigned. The DCC will issue new lists periodically.

1. Early onset septicemia/bacteremia (≤ 72 hrs)?

Code 'Y' if there was a positive blood culture drawn within the first 72 hours. Code 'N' otherwise.

a. If YES, organism code(s):

Record the code(s) of organism(s) identified. If there were more than two organisms identified, list the organisms felt to be most important.

2. Did the infant receive antibiotics for ≥ 5 days, starting within the first 72 hours?

Code 'Y' if the infant was treated with antibiotics for five or more days beginning by 72 hours. Include cases where the infant died before an intended therapy of five or more days was completed. Code 'N' otherwise.

a. If YES, reason:

Code reason antibiotics were given:

- 1 = Sepsis
- 2 = Meningitis
- 3 = UTI
- 4 = Pneumonia
- 5 = Other

3. Number of episodes of late onset blood culture negative clinical infection (> 72 hours to status) treated with antibiotics for ≥ 5 days?

Record the number of blood culture negative episodes, occurring after 72 hours, treated with antibiotics for five or more days. Include cases where the infant died before an intended therapy of five or more days was completed.

4. Late onset blood culture positive septicemia/bacteremia (> 72 hrs)?

Code 'Y' if there was a positive blood culture, obtained in the presence of compatible clinical signs of septicemia, occurring after 72 hours, treated with antibiotics for ≥ 5 days. Include blood culture positive episodes in which the infant dies before an intended therapy of five or more days is completed. A new organism cultured at any time is considered an additional episode. If the same bacterial organism is cultured after 10 days of appropriate antibiotic therapy, this is considered a new episode. There are only 6 entries on the form, however, the DMS will accept up to 10 entries. Code 'N' otherwise.

If YES,

For each episode (a), record the start and stop date (b1 and b2), organism code(s) (c1-c3), and whether there was Central Line Associated Blood Stream Infection (CLABSI) (d) (record 'Y' or 'N') from positive blood culture(s) for which the infant was treated, or where there was intent to treat for ≥ 5 days. The stop date is the last day of antibiotics. A **Central Line Associated Blood Stream Infection (CLABSI)** is a laboratory-confirmed bloodstream infection (BSI) in a patient who had a central line within the 48 hour period before the development of the BSI and that is not related to an infection at another site. If more than 3 organisms are identified, list the 3 organisms felt to be the most important. If the same organism is isolated under the circumstances described in a. (above), the code is repeated.

e. If late onset sepsis, was creatinine measured?

Code 'Y' if at least one serum creatinine was measured within the 10 day period after initial diagnosis. Code 'N' otherwise.

1. If YES, highest value

Record the highest serum creatinine level obtained.

2. If YES, Date

Record the date the highest serum creatinine level was measured.

5. Was the infant diagnosed with UTI?

Code 'Y' if infant was diagnosed with a urinary tract infection (UTI). Code 'N' otherwise.

1. If YES, Organism

Code organism associated with the UTI. **Use Appendix A to obtain code(s) for identified organism(s).**

2. If YES, Date

Record the date the UTI was diagnosed.

6. Did the infant have an LP as part of a sepsis evaluation (not for hydrocephalus)?

Code 'Y' if the infant had a lumbar puncture performed as part of a septic work up. Exclude an LP performed for a ventricular tap for hydrocephalus. There are 5 fields on the form, however, the DMS will accept up to 10 fields. Code 'N' otherwise.

If YES, a. Record date(s) lumbar puncture performed. Record up to 5 LPs.

7. Meningitis?

Code 'Y' if there was a positive cerebrospinal fluid (CSF) culture and treatment (or intent to treat) with antibiotics or antifungals for 7 or more days. Code 'N' otherwise.

If YES,

Organism code(s):

For each episode number (a) record the date, (b) code(s) of organism(s) (1, 2, 3) identified, and (c) if the episode was confirmed by PCR. If there were more than three organisms identified, list the three organisms felt to be most important.

Use Appendix A to obtain code(s) for identified organism(s).

8. Was the infant diagnosed with any of the following other proven infections?

Code 'Y' if the infant was diagnosed with any of the following other proven infections listed below. Code 'N' otherwise.

If YES:

For each diagnosis number (ar) record (b) Date of Diagnosis and (c) Diagnosis code.

Code:

- 1 = Neonatal herpes
- 2 = Congenital CMV (diagnosed \leq 3 weeks old)
- 3 = Acquired CMV (diagnosed $>$ 3 weeks old)
- 4 = Congenital syphilis
- 5 = Congenital toxoplasmosis
- 6 = HIV infection

9. Was a congenital infection diagnosed?

Code 'Y' if a congenital infection was diagnosed. Code 'N' otherwise.

If YES,:

a. Organism?

Code organism associated with the congenital infection. **Use Appendix A to obtain code(s) for identified organism(s).**

b. Treated

Code 'Y' if the infant was treated for a congenital infection. Code 'N' otherwise.

4.3.16 Section P – SYNDROMES AND/OR MALFORMATIONS

1. Syndromes and/or major malformations?

Code 'Y' if any syndromes and/or major malformations were diagnosed, including Down syndrome, chromosomal abnormalities, and other syndromes with multi-organ involvement. Code 'N' otherwise.

- a. If YES, **code**
Record the code(s) of the syndromes and/or major malformations diagnosed. The syndrome/major malformation codes are listed in **Appendix H: Birth Defect Codes**.
- b. **If a syndrome is coded as 'Other', specify**
Document the specific name of the syndrome. 'Other' codes include 199, 299, 399, 499, 599, 699 and 799, according to system involvement.

4.13.17 Section Q – SURGERIES AND CATHETERIZATION PROCEDURES

1. **Did the infant have surgery or catheterization procedure?**

Code 'Y' for all surgical procedures and/or catheterization procedures that occurred prior to status, including PDA ligation and/or surgery for ROP. Code "N" otherwise.

- a. If YES, record the date (i), all surgical codes (ii) for procedures performed on that date, and if there was surgical site infection (iii) for each surgery

i. **Date (mm/dd/yyyy)**

Record date of surgery.

ii. **Surgery code(s)**

See **Appendix E** for major surgery codes. There are 6 entries on the form, however, the DMS will accept up to 10 entries. Failed catheterization closures should also be included.

iii. **Surgical Site Infection?**

Code 'Y' if there was a surgical site infection. Code 'N' if there was not a surgical site infection. Code 'Unk' if this information is not known.

- b. **If a surgery is coded as 'Other' (codes ending in 99), specify**

Record the specific name of the surgery performed.

If surgery is coded as "703" answer Q1c.

- c. Code 'Y' if the infant received any new vasoactive drugs within 24 hours after PDA closure (ligation or catheterization) . Code 'N' otherwise.

4.4 NG03E: GENERIC EARLY DEATH FORM

4.4.1 NG03E Form Questions – Section A – Early Death

Complete this form if the infant died at \leq 12 hours of age. This includes infants who died in the delivery room.

1. **Medical therapy initiated**

Code 'Y' to all medical therapies that were initiated anytime after birth. Code 'N' otherwise.

- a. **Antibiotics?**

- b. **Surfactant replacement therapy?**

If YES, record the following:

1. Type of surfactant given:

Record the type of surfactant given:

- 1 = Beractant (Survanta)
- 2 = Poractant alfa (Curosurf)
- 3 = Calfactant (Infasurf)
- 9 = Other

2. Was the surfactant mixed with budesonide?

Code 'Y' if the surfactant administered was mixed with budesonide. Code 'N' if otherwise. Code 'T' if the infant was enrolled in the BiB trial. If 'TI' refer to section 3.2.1 for detailed instructions.

3. Method of administration:

Record the method of administration:

- 1 = ETT (endotracheal tube) – includes INSURE (INTubate, SURFactant, REmove) given using an endotracheal tube
- 2 = LISA/MIST (less invasive surfactant administration or minimally invasive surfactant treatment) – defined by use of a specialized catheter used to inject surfactant below the vocal cords
- 3 = Aerosolized – may be given using a nebulizer via mask or prongs
- 4 = LMA (laryngeal mask airway)
- 9 = Other

c. Pressor support?

This includes dopamine, dobutamine, epinephrine and isuprel.

d. Volume support?

This includes albumin 5% or 20%, blood transfusion, fresh frozen plasma, plasmanate and Ringer's lactate.

e. Intubation and Ventilation?

Code 'Y' if infant was intubated and received mechanical ventilation with an endotracheal tube in place.

f. IV fluids?

2. Autopsy performed?

Code 'Y' if an autopsy was performed. If an autopsy is performed the cause of death should not be coded until the results of the autopsy are known. The NG03E should not be held back for coding or entry into the EDC waiting for the autopsy report. If the autopsy result for cause of death is to be included and results are not yet available, enter the temporarily missing data code 'TM', and enter final autopsy cause of death in the EDC when it becomes available.

3. At any time after birth (prior to NG03E Status), was there documentation of discussion with parents to limit, withdraw or not escalate care?

Code 'Y' if there is documentation of discussion with parents to limit, withdraw or not escalate care. Otherwise code 'N.'

4. **Were the following treatments withheld, limited or withdrawn at any time with the intent to limit care?**

a. Intubation/ventilation

Code 'Y' if intubation or ventilation was withheld, limited or withdrawn at any time with the intent to limit care. Code 'N' otherwise.

b. Nutrition/hydration

Code 'Y' if nutrition or hydration was withheld, limited or withdrawn at any time with the intent to limit care. Code 'N' otherwise.

5. **Palliative care consult obtained?**

Code 'Y' if palliative care consult was obtained. Code 'N' otherwise.

6. **Ethics consult obtained?**

Code 'Y' if an ethics consult was obtained. Code 'N' otherwise.

7. **No intention to resuscitate (comfort care only)**

Code 'Y' if there was no intention to resuscitate and only comfort care was provided. Code 'N' otherwise.

8. **Contributory cause of death:**

This should be the underlying, proximate disease which initiated the series of events leading to the cause of death. This underlying cause must be (1) etiologically specific and (2) antecedent to all other causes with respect to time and pathologic relationship. Without the underlying cause, death would not have occurred. The cause of death should be based on both clinical evidence and autopsy findings. In the absence of an autopsy, the clinical evidence will be used. Only one option is coded after consultation with the PI or alternate PI.

A list of the causes of death are in **Appendix C**.

9. **If contributory cause of death is code 10 (Congenital malformation) or code 90 (Other), specify:**

NG05: LATE CLINICAL OUTCOME FORM

4.5 Coding Instructions for Form NG05

The NG05 is to be completed for infants who are hospitalized greater than 120 days and reach status (death, discharge, transfer or one year postnatal age). The NG05 collects diagnosis and treatments that occur after day of life 120.

4.5.1 Section A - STATUS

1. **Status of infant at time of completion of form**

1 = if infant was discharged to home

3 = if infant was transferred to another facility (including hospital, chronic care facility or hospice facility, etc.) without returning in 7 days

5 = if the infant died

6 = if the infant remains in hospital after one year postnatal age

2. **Date of status**

Record date of status.

3. **Weight at status**

Weight in grams at status (preferably), or within 7 days.

4. **Length at status**

Length in centimeters at status (preferably), or within 7 days.

5. **Head circumference at status**

Head circumference in centimeters at status (preferably), or within 7 days.

4.5.2 *Section B - EXTENDED STAY INFORMATION*

1. **What problem (s) caused hospitalization greater than 120 days:**

Answer 'Y' to all that apply. Answer 'N' otherwise.

a. **Pulmonary?**

b. **Cardiac?**

c. **Neurologic?**

d. **Gastrointestinal?**

e. **Multiple Malformations?**

f. **Social?**

g. **Ophthalmologic?**

h. **Sepsis/Infection?**

i. **Renal?**

j. **Apnea?**

k. **Feeding?**

l. **Other? (If Yes, specify)**

2. **Did either eye receive therapy for ROP after 120 days?**

Code 'Y' if either eye received therapy for ROP after 120 days. Code 'N' otherwise.

a. If YES or Trial **List all therapies done for either eye (Use codes below):**

1 = laser

2 = cryotherapy

3 = scleral buckle

4 = vitrectomy

5 = avastin or anti-VEGF

6 = other (specify) for either eye

If initial treatment/medication is given under a masked or unmasked study protocol or if subsequent treatment/medication is received as part of clinical care post trial, refer to Section 3.2.1 for detailed instructions.

3. Was a hearing screen performed after 120 days?

Code 'Y' if a hearing screen was performed after 120 days to evaluate the infant's hearing while in the hospital. Code 'N' otherwise.

If YES,

a. Was otoacoustic emissions (OAE) testing performed?

Code 'Y' if OAE testing was performed. Code 'N' otherwise.

If YES,

1. Was OAE failed?

Code 'Y' if infant failed the OAE. Code 'N' otherwise.

If YES,

i. Unilateral or bilateral fail?

Code

1=Unilateral

2=Bilateral

b. Was automated auditory brainstem response (AABR) performed?

Code 'Y' if automated auditory brainstem response (AABR) was performed. Code 'N' otherwise.

If YES,

1. Was AABR failed?

Code 'Y' if infant failed the AABR. Code 'N' otherwise.

If YES,

i. Unilateral or bilateral fail?

Code

1=Unilateral

2=Bilateral

4. Was a diagnostic auditory brainstem response (ABR) performed prior to discharge?

Code 'Y' if there was documentation of an ABR performed prior to discharge. Code 'N' otherwise.

If YES,

a. Was hearing loss documented?

Code 'Y' if hearing loss was documented. Code 'N' if no hearing loss was documented. Code 'Unk' if report not available to make determination.

If YES,

b. Unilateral or bilateral hearing loss?

Code

1=Unilateral
2=Bilateral

4.5.3 Section C - ETHICS/PALLIATIVE CARE

1. **Was there documentation of discussion with parents to limit, withdraw or not escalate care after 120 days?**

Code 'Y' if after 120 days, there was documentation of a discussion with parent to limit, withdraw or not escalate care. Code 'N' otherwise.

2. **Were the following treatments withheld, limited or withdrawn after 120 days with the intent to limit care?**

Code 'Y' to all that apply. Code 'N' otherwise.

a. **Intubation/ventilation**

b. **Nutrition/hydration**

3. **Palliative care consult was obtained?**

Code 'Y' if there was documentation that a palliative care consult was obtained. Code 'N' if otherwise.

4. **Ethics consult was obtained?**

Code 'Y' if there was documentation that an ethics consult was obtained. Code 'N' if otherwise.

4.5.4 Section D - TRANSFER

This section refers to when the infant is sent to another hospital or chronic care facility without returning in 7 days. Complete this section if status of infant is "transferred."

1. **Date of transfer:**

Record date of transfer

2. **Final outcome:**

Code the final outcome:

1 = if the baby died in hospital (informed via telephone contact or letter from the other hospital)

2 = if the baby was discharged to home

3 = if the baby remains in the hospital at one year of age

4.5.5 Section E - DISCHARGE ALIVE

Complete this section if the Status of the infant is 1 =discharged home'

1. **Date of discharge to home**

Record date of discharge.

2. **Discharged home on continuous oxygen?**

Code 'Y' if discharged home on continuous oxygen. Code 'N' otherwise.

3. **Discharged home on any of the following medications?**

Code 'Y' if infant is discharged home on any medication(s) listed below. Otherwise code 'N.' For questions 3.a.-3.g., code 'Trial' if infant discharged on a trial medication in a masked placebo controlled study. Refer to section 3.2.1 for details.

- a. **Diuretics**- including but not limited to furosemide, spironolactone, chlorothiazide, or hydrochlorothiazide
- b. **Bronchodilators**- including but not limited to albuterol
- c. **Anticonvulsants** including but not limited to phenobarbital, dilantin, valproic acid, depakane, carbamapepzine
- d. **Antireflux medications**- including but not limited to ranitidine, famotidine, metaclopramide.
- e. **Antihypertensive medications** including but not limited to hydrazaline.
- f. **Methylxanthines** - including but not limited to caffeine, theophylline, and aminophylline.
- g. **Inhaled steroids** - including but not limited to budesonide (pulmicort) and fluticasone (flovent).
- h. **Systemic steroids** – including but not limited to dexamethasone, hydrocortisone, and prednisone/prednisolone.
- i. **Other, specify**
Specify other medication on which infant was discharged home. Do not include multivitamins or iron.

4. Discharged home receiving any human milk?

Code 'Yes' (complete D4a) if infant is discharged home receiving any human milk. Otherwise answer "no or Unknown."

a. If YES, type of milk

Code the type of milk:

- 1= Maternal Milk
- 2= Donor Milk
- 3= Both
- 4= Unknown

4.5.6 Section F - DEATH

Complete this section if the Status of the infant is '5=Death'

1. **Date of death:**
Record date of death.
2. **Autopsy performed?**
Code 'Y' if an autopsy was performed. If an autopsy is performed, the cause of death should not be coded until the results of the autopsy are known. Code 'N' otherwise.
3. **Contributory cause of death:**
This should be the underlying, proximate disease which initiated the series of events leading to death. This underlying cause must be (1) etiologically specific and (2) antecedent to all other causes with respect to time and pathologic relationship. Without the underlying cause, death would not have occurred. The cause of death should be based on both clinical evidence and autopsy findings. In the absence of an autopsy, the clinical evidence will be used. Only one option is coded after consultation with the PI or alternate PI.

A list of the causes of death are in **Appendix C**.

4. **If cause of death is code 10 (Congenital malformation), code 31 (Sepsis, specify organism), or code 90 (Other), specify.**

Chapter 5 THE RESPIRATORY SUPPORT DATA

5.1 The Respiratory Support data on the NG07

5.1.1 Respiratory Support Form Overview

The NG07 form is completed for all GDB infants who have survived for greater than 12 hours and have reached status (death, discharge, transfer or 120 days). Respiratory support the infant received during the hospitalization is documented at the time points noted. For any infant who survived >12 hours but death occurred <24 hours, data is completed in the Status column only. If Status (death, discharge or transfer) is reached before any time point, some column(s) will be left blank. The Status column will always be completed to give the total number of days for each type of respiratory support and oxygen during the hospitalization.

The NG07 also collects information to define the outcome of bronchopulmonary dysplasia (BPD) for infants in the GDB. Infants enrolled in the PDA Trial or the BiB Trial will be evaluated for their eligibility for the Physiologic Evaluation and the results of this evaluation, if performed, will be documented. The Jensen BPD criteria (see Appendix M) will be used to standardize the definition and grade of BPD for infants in the GDB and for any protocol which has a primary or secondary outcome of BPD except for the PDA Trial and the BiB Trial, which will continue to use the Physiologic Definition of BPD.

5.1.2 Section A - RESPIRATORY SUPPORT

Respiratory Support data is collected as follows:

Questions A1. through A5.:

1. **Number days on HFV**
2. **Number days on CV**
3. **Number of days on nasal ventilation**
4. **Number days on CPAP**
5. **Number of days on supplemental O₂**
6. **Highest FiO₂ on day**
7. **Highest mode of support on day, code**
 - 1 = HFV
 - 2 = CV
 - 3 = Nasal ventilation
 - 4 = CPAP
 - 5 = NC
 - 6 = Hood
 - 7 = No Support
 - 8 = Temporarily out of unit
8. **If mode '5', record Flow Rate**
9. **Weight (grams)**

The respiratory support box collects FiO_2 and mode of support **at** 24 hours of life (snapshot **at** 24 hours of life) and cumulative data, recording the total number of days for each type of respiratory support across a row at each time point days 3, 7, 14, 28, 36 weeks' PMA and Status) during hospitalization. If Status is reached before any time point(s), no data will be entered for the time point(s) that would occur after the date of Status. The last entry will always be Status.

Respiratory support is collected using a hierarchy, counting only the highest type of respiratory support (HFV, CV, Nasal ventilation, CPAP, Nasal Cannula, Hood) for any given day. **The hierarchy for respiratory support is HFV as highest, next CV, nasal ventilation, CPAP, nasal cannula, hood.** If an infant is on multiple modes of support on any day, only the highest level would count for that day.

Example: If the infant was receiving conventional ventilation (CV) and high frequency (HFV) on the same calendar day, count only the HFV for that day.

Modes of support are HFV (including oscillator, jet), CV (including IMV, SIMV and/or assist control via an endotracheal tube), nasal ventilation (via nasal prongs or cannula), CPAP (nasal prongs, cannula or mask), and supplemental oxygen (delivered by any method including ventilator, CPAP, nasal cannula, hood or incubator).

The day of birth is considered day of life 1 even though it is not a complete 24 hour period. Day of life 2 is the next calendar day.

The total number of days of all support cannot exceed the day of life.

Example: On day 7, the infant may have received 4 days of CV and 2 days nasal ventilation and 1 day CPAP for a total number of days of support to equal 7 days. The infant could receive less than 7 days if there was no respiratory support on any of the first 7 days.

Questions A.6. and A.7.:

The highest FiO_2 and highest mode of support are recorded for each time point.

Question A.6. Record the highest FiO_2 delivered any time during the day (by HFV, CV, nasal ventilation, CPAP, nasal cannula or hood) at 24 hours of life, days 3, 7, 14, 28, 36 weeks' PMA and Status. When determining the highest FiO_2 for each day, disregard any temporary increases in FiO_2 for desaturation episodes, apnea, bradycardia or procedures, when the infant returns to the previous FiO_2 in a reasonable amount of time (<2 hours). DO NOT include supplemental oxygen given only with feedings if the infant is not receiving oxygen at any other time during that day.

Question A.7. Record the highest mode of support the infant received on each day using the codes listed on the form. If the infant is on more than one mode of support, use the hierarchy (HFV as highest, CV next, nasal ventilation, next then CPAP, nasal cannula, hood) to record the mode of support for that day. Additionally:

1. Respiratory support delivered by nasal mask or prongs that is only flow is coded as CPAP.
2. Respiratory support delivered by nasal mask or prongs that delivers flow and intermittent breaths is Nasal ventilation.

Question A.8. Record the flow rate if nasal cannula (code=5) is recorded as the highest level of support on any day. The flow rate recorded is the flow delivered with the highest FiO_2 on that day.

Example: If any time during a day, the infant was on FiO_2 1.00 with flow rate 0.03 lpm and also during that day was switched to an FiO_2 .27 with a flow rate of 0.5 lpm, record FiO_2 1.00, flow 0.03 lpm.

Any GDB infant that is enrolled in the PDA Trial or the BiB Trial should be evaluated for physiologic challenge eligibility **if on day of 36 weeks (A.6. 36 weeks) the highest mode of support (A.7.) is answered 5 = nasal cannula with or without supplemental oxygen or 6 = hood (to include oxygen delivered into an incubator).** Supplemental oxygen requirements should be determined with the infant at rest. Disregard any temporary increases in oxygen requirement (for desaturation episodes, apnea, bradycardia or procedures, when the infant returns to baseline oxygen in a reasonable amount of time (<2 hours)). Do not include supplemental oxygen given only with feeds.

If the Section 'A - 36 weeks' question 7 is NOT answered with mode = 5 or 6, **the infant should NOT be evaluated for physiologic challenge eligibility** and the form is complete.

Question A.9. Record the infant's weight at each time point. The following windows may be used for each time point:

- Day 3: (weight collected between day 2 and day 4)
- Day 7: (weight collected between day 6 and day 8)
- Day 14: (weight collected between day 12 and day 16)
- Day 28: (weight collected between day 26 and day 30)
- 36 weeks: (weight collected between 36-0/7 to 37-0/7 weeks)

5.1.2 Section B - PHYSIOLOGIC CHALLENGE ELIGIBILITY

Physiologic challenge eligibility should only be conducted on infants enrolled in the PDA Trial or the BiB Trial and if Section 'A - 36 weeks' question 7 is answered with mode = 5 or 6.

1. Is infant enrolled in the PDA Trial or the BiB Trial?

If **NO**, the infant is not enrolled in the PDA Trial or the BiB trial, then the infant is not eligible and the form is complete.

If **YES**, proceed to question B1a.

To determine eligibility for the Physiologic Challenge:

An **Effective FiO_2** will be calculated for infants receiving supplemental oxygen by nasal cannula using the infant's weight, flow (lpm) and oxygen concentration. Conversion tables in **Appendix J** are included to determine the **Effective FiO_2** .

The actual FiO_2 concentration will be used for infants receiving oxygen by hood (including oxygen delivered into an incubator).

If eligibility criteria are met, the infant's chart will be reviewed for oxygen saturation readings in the prior 24 hours. The 'majority' of saturations is defined as >90% of saturation readings during the prior 24 hour period.

Any infant deemed eligible will have a physiologic challenge performed.

The protocol for the Physiologic Definition of Bronchopulmonary Dysplasia is included as **Appendix J**.

a. Weight on day of 36 weeks

Record the infant's weight in grams on day of 36 weeks' post menstrual age.

b. Is the infant eligible for a physiologic challenge?

Infants eligible for a physiologic challenge must meet one of the following:

- Effective oxygen <27% AND majority of saturations \geq 90%
- Effective oxygen 27%-30% AND majority of saturations \geq 96%
- Room air by nasal cannula.

c. Was the physiologic challenge performed?

If YES,

1. Date of challenge

2. Did the infant pass challenge?**

See Physiologic Definition of BPD protocol (Appendix J**)

3. Reason not performed (use codes)

1 = Increased FiO_2

Infant's supplemental oxygen requirement has increased and is no longer eligible

2 = Increased respiratory support-

Infant has been placed on CPAP or ventilator and is no longer eligible

3 = Instability

To include, but not limited to surgery, sepsis where the infant may not tolerate the challenge

4 = Parent/Physician refusal

5 = Weaned to room air on/before day of evaluation/challenge

No longer eligible because no longer requiring supplemental oxygen and is not receiving any respiratory support.

9 = Other- Explain

Chapter 6

6.1 The COVID-19 data on the NG09

6.1.1 COVID-19 Form Overview

The NG09 form is completed for all GDB infants beginning with births on March 1, 2020. The form collects COVID-19 related information on exposure and testing in both the mother and infant. The form should be completed from time of birth until NG03 Status is reached.

6.1.2 Section A – MATERNAL INFORMATION

1. Was the mother tested for active SARS-CoV-2 infection?

Code 'Y' if the mother was tested for active SARS-CoV-2 infection during the pregnancy through delivery hospitalization. Test may be any molecular assay such as PCR (or antigen detection) but not antibody/serologic testing (see below). Code 'N' if the mother was not tested for active SARS-CoV-2 infection during the pregnancy through delivery hospitalization. Code 'Unk' if it is not known if the mother was tested for active SARS-CoV-2 infection during the pregnancy through delivery hospitalization. Record this information for each test that was administered.

If YES,

a. Test Number

Record the test number.

b. Test Result

Code the SARS-CoV-2 test result:

- 1 = Positive
- 2 = Negative
- 3 = Inconclusive

c. Type of Test:

Code the type of test that was administered. Record 'Unk' if the type of test administered is unknown.

Code:

- 1 = Lab/pharmacy test
- 3 = At-home test
- 4 = Unknown

d. Reason(s) for Testing?

Code the reason(s) the mother was tested for SARS-CoV-2. Code 'Unk' if otherwise.

- 1 = Symptomatic
- 2 = Exposure
- 3 = Screening
- 4 = Other

e. Date of Test

Record date SARS-CoV-2 test was performed. Record 'Unk' if the date SARS-CoV-2 test was performed is not known.

If UNKNOWN,

f. Testing Time Period

Complete this question only if the exact date of testing is unknown.

Code the time period during which the test occurred:

- 1 = During pregnancy** – any time during pregnancy that mother is tested before the delivery admission
- 2 = At delivery** – when the mother presents for delivery and before the birth of the infant
- 3 = Postpartum** – after the birth of the infant before the mother is discharged home
- 4 = Unknown**

2. Was the mother tested for SARS-CoV-2 antibodies?

Code 'Y' if the mother was tested for SARS-CoV-2 antibodies during the pregnancy through delivery hospitalization. Code 'N' if the mother was not tested for SARS-CoV-2 antibodies during the pregnancy through delivery hospitalization. Code 'Unk' if it is not known if the mother was tested for SARS-CoV-2 antibodies during the pregnancy through delivery hospitalization. Record this information for each test that was administered.

If YES,

b. Test Result

Code the SARS-CoV-2 antibody test result (even if the date of test is unknown):

- 1 = Positive
- 2 = Negative
- 3 = Inconclusive

c. Date of Test

Record date SARS-CoV-2 antibody test was performed. Record 'Unk' if the date SARS-CoV-2 antibody test was performed is not known.

If UNK,

d. Testing Time Period

Complete this question only if the exact date of testing is unknown.

Code the time period during which the test occurred:

- 1 = During pregnancy** – any time during pregnancy that mother is tested before the delivery admission
- 2 = At delivery** – when the mother presents for delivery and before the birth of the infant
- 3 = Postpartum** – after the birth of the infant before the mother is discharged home
- 4 = Unknown**

6.1.3 Section B – INFANT INFORMATION

1. Was the infant tested for active SARS-CoV-2 infection?

Code 'Y' if infant was tested for active SARS-CoV-2 infection. Test may be any molecular assay such as PCR (or antigen detection) or serology. Code 'No' if infant was not tested for active SARS-CoV-2 infection. Code 'Unk' if it is not known if the infant was tested for active SARS-CoV-2 infection. Record this information for each test that was administered.

If YES,

b. Test Result

Code the SARS-CoV-2 test result:

- 1 = Positive
- 2 = Negative
- 3 = Inconclusive

c. Type of Test:

Code the type of test that was administered. Code:

- 1 = Molecular assay (e.g. PCR) or Antigen detection
- 2 = Serology: IgM

d. Date of Test

Record the date the infant was tested for SARS-CoV-2 infection. Record 'Unk' if the date test was performed is not known.

e. Reason(s) for Testing

Code the reason(s) for testing. Code all that apply:

- 1 = Mother suspected or has COVID-19
- 2 = Infant thought to be exposed to someone besides mother with COVID-19, e.g. father, sibling, healthcare worker
- 3 = Infant had clinical signs consistent with infection that might include COVID-19 infection
- 4 = Screening
- 5 = Other, specify

f. Sample Site

Code the sample site for the test. Code all that apply:

- 1 = Nasopharynx
- 2 = Oropharynx (throat)
- 3 = Stool/rectum
- 4 = Tracheal aspirate
- 5 = Serum/blood
- 6 = Other (name site)

Chapter 7

Revisions/Additions to the GDB

7.1 Overview

It is recognized that changes (additions, deletions, revisions) to the GDB will be necessary periodically. Such changes may be: 1) permanent changes to the core GDB; or 2) time-limited data collection for studies which relate to areas of special interest. All proposed changes to the GDB must undergo thorough, prospective and formal review to determine whether the proposed changes are appropriate and acceptable. Historical changes are recorded in a separate document.

The core GDB is a limited data set which represents important/essential information (which is expected to change over time) for all VLBW infants. The core GDB is not intended to include detailed data on areas of special interest in the VLBW population. Such data, in sufficient detail to provide meaningful information, can be collected as an addendum to the core GDB after appropriate approval.

It is the understanding of the GDB Subcommittee that areas of special interest generally lend themselves to data collection for a finite period of time, i.e. special interest data collection forms are not considered part of the core GDB. The process for proposing changes to the GDB, either permanent or temporary, is described in Section 7.2

7.2 Process of Proposing Revisions/Additions to the GDB

All proposed changes to the GDB must be submitted as a formal proposal to the Protocol Review Subcommittee (PR Subcommittee).

The Chair of the PR Subcommittee will determine whether the proposal is acceptable (contains all information required for review as identified by policies established by the Protocol Review Subcommittee). The Chair will also determine whether the proposal requires full review by the PR Subcommittee or whether it may be reviewed by the GDB Subcommittee (without prior full review by the PR Subcommittee).

If a proposal is reviewed and approved by either the PR or the GDB Subcommittee, the proposal will be reviewed by the Steering Committee for final approval prior to implementation.

Appendix A Organism Codes List

Code	Genus	Species
<u>Bacteria</u>		
310	Achromobacter	sp. [inc. Achromobacter xylooxidans and others]
320	Acinetobacter	sp. [antiratus, baumannii calcoaceticus, haemolyticus, johnsonii, junii, lwoffii, radioresistens]
330	Aeromonas	sp.
340	Alcaligenes	sp. [Alcaligenes xylooxidans and others]
140	Bacillus	sp.
410	Bacteroides	sp.
160	Bifidobacterium	sp. [Bifidum, lactis, infantis, thermophilum, and others]
350	Burkholderia	sp. [Burkholderia capecica and others]
360	Campylobacter	sp. [Campylobacter fetus, C. jejuni and others]
620	Chlamydia	trachomatis
370	Chryseobacterium	sp.
226	Citrobacter	sp. [Citrobacter diversus, C. freundii, C. koseri and others]
420	Clostridia	sp.
500	Corynebacterium	sp.
240	Enterobacter	sp. [Enterobacter aerogenes, E. cloacae, and others]
380	Enterococcus	sp. [Enterococcus faecalis (a.k.a. Streptococcus faecalis and Streptococcus Group D), E faecium, and other Enterococcus species]
200	Escherichia	coli
390	Flavobacterium	sp.
590	Haemophilus	sp. [Haemophilus influenzae, H. vaginalis and others]
325	Herellea	vaginicola
230	Klebsiella	sp. [Klebsiella oxytoca, K. pneumoniae and others]
170	Lactobacillus	sp. [Acidophilus, casei, and others]
150	Listeria	sp. [Listeria monocytogenes]
105	Micrococcus	sp.
430	Moraxella	sp. [Moraxella catarrhalis (a.k.a. Branhamella catarrhalis) and others]
650	Morganella	morganii
640	Mycobacterium	sp. [tuberculosis]
570	Neisseria	sp. [Neisseria meningitides, N. gonorrhoeae and others]
440	Pasteurella	sp.
460	Peptostreptococcus	sp.
480	Prevotella	sp.

470	Propionibacterium	sp.
260	Proteus	sp. [Proteus mirabilis, P. vulgaris and others]
300	Pseudomonas	sp.
301	Pseudomonas	aeruginosa
210	Salmonella	sp.
250	Serratia	sp. [Serratia liquefaciens, S. marcescens odorifera, ficara, plymuthica and others]
101*	Staphylococcus	aureus [coagulase positive]
104	Staphylococcus	coagulase negative (including S. epidermis, saprophyticus, haemolyticus, hominis, lugdunensis, simulans, cohnii, warnei, saccharolyticus)
510	Stenotrophomonas	maltophilia
111	Streptococcus	viridans
112	Streptococcus	Group A
113	Streptococcus	Group B

*Note- call lab if unclear whether staphylococcus is coagulase negative, coagulase positive, aureus or epi.

133	Streptococcus	pneumoniae
561	Treponema	pallidum [syphilis]
610	Vibrio	
600	Yersinia	
699	Other; Code to be assigned	

Fungi

834	Aureobasidium	sp.
810	Candida	sp.
811	Candida	albicans
813	Candida	krusei
816	Candida	parapsilosis
817	Candida	tropicalis
819	Candida	glabrata
820	Candida	guilliermondi
821	Candida	lusitaniae
881	Malassezia	fur
872	Saccharomyces	sp. [yeast]
899	Other; Code to be assigned	

Resistant Organisms

750	Methicillin resistant staphylococcus aureus (MRSA)
760	Vancomycin resistant enterococci (VRE)

Viruses

901	Cytomegalovirus
903	Enteroviruses [includes coxsackie, echoviruses]
920	Hepatitis A
923	Hepatitis B

924	Hepatitis C	
905	Herpes Simplex	
907	HIV	
910	Rubella	
960	Varicella	zoster

Other Organisms

911	Toxoplasma	gondii [toxoplasmosis]
010	Other; Code to be assigned	

Appendix B Drug Therapeutic Agent List

Penicillins

- 01 = Ampicillin
- 02 = Carbenicillin
- 03 = Oxacillin
- 04 = Penicillin G
- 05 = Piperacillin
- 06 = Ticarcillin
- 07 = Mezlocillin
- 08 = Methicillin
- 09 = Nafcillin
- 10 = Amoxicillin
- 11 = Amoxicillin/clavulanate (Augmentin)

Cefalosporins

- 19 = Cephalexin (Keflex)
- 20 = Cephalothin
- 21 = Cefazolin (Kefzol)
- 22 = Cefotaxime (Claforan)
- 23 = Cefoxitin
- 24 = Moxalactam
- 25 = Ceftazidime (Fortaz)
- 26 = Ceftriaxone (Rocephin)
- 27 = Ceftizoxime
- 28 = Cefuroxime
- 29 = Cefotetan
- 30 = Cefixime

Aminoglycosides

- 31 = Amikacin
- 32 = Gentamicin
- 33 = Kanamycin
- 34 = Tobramycin

Other Antibiotics

- 44 = Vancomycin
- 46 = Bactrim
- 47 = Chloramphenicol (Chloromycetin)
- 49 = Clindamycin
- 50 = Erythromycin

Other Antibiotics (continued)

- 62 = Imipenem
- 63 = Metronidazole
- 64 = Aztreonam
- 67 = Ampicillin + sulbactam (unasyn)
- 68 = Azithromycin
- 70 = Cefepime
- 75 = Meropenem
- 76 = Piperacillin + tazobactam (zosyn)
- 77 = Rifampin
- 78 = Ticarcillin + clavulanate
- 80 = Ciprofloxacin
- 81 = Clarithromycin (Biaxin)
- 82 = Doxycycline
- 83 = Trimethopim/sulfa (TMP/SMX)
- 91 = Linezolid

Antifungals

- 43 = Flucytosine (5FC)
- 48 = Nystatin
- 61 = Fluconazole
- 69 = Caspofungin
- 92 = Itraconazole
- 93 = Posaconazole
- 94 = Voriconazole
- 41 = Amphotericin B
- 66 = Amphotericin B Liposome (Ambisome)
- 95 = Amphotericin B lipid complex (Abelcet)
- 97 = Anidulafungin
- 98 = Micafungin

Antivirals

- 45 = Vidarabine
- 71 = Acyclovir (Zovirax)
- 72 = Ganciclovir
- 73 = Nevarapine
- 74 = Zidovudine (AZT)
- 96 = Valacyclovir hydrochloride (Valtrex)

Other Drugs Not Listed

- 99 = Other

Appendix C Causes of Death

Malformation

10 - Congenital malformation

Code '10' for major congenital malformations that are incompatible with life, or incompatible with life without drastic surgical or other measures to maintain life such as a chromosomal defect, inborn error of metabolism, neural tube defect, congenital heart disease, or renal abnormality. If an infant has respiratory distress syndrome or intracranial hemorrhage but is allowed to die because his/her main problem is the congenital malformation, then malformation should be coded as the cause of death.

Pulmonary

20 - RDS

Code '20', RDS, for severe respiratory insufficiency in the presence of RDS during the first 28 days of life, i.e., increasing oxygen and ventilatory pressure requirements, pneumothorax, pneumopericardium, etc.

21 - RDS with severe intracranial hemorrhage

Code '21' for infants with severe respiratory insufficiency in the presence of RDS during the first 28 days of life with severe (grade III-IV) intracranial hemorrhage.

22 - RDS with infection

Code '22' for infants with severe respiratory distress in the presence of RDS during the first 28 days who have a fulminant pulmonary or other infection. For example, if an infant has group B streptococcal sepsis with a clinical presentation of respiratory distress, or respiratory distress syndrome with an intercurrent infection, then RDS with infection should be coded as the cause of death.

23 - RDS with massive pulmonary hemorrhage

Code '23' for infants with respiratory distress syndrome diagnosed during the first 28 days of life and massive pulmonary hemorrhage.

25 - BPD

Code '25', for infants with chronic lung disease requiring respiratory support (nasal cannula, CPAP, or positive-pressure ventilation, either noninvasive or invasive) at 36 weeks' postmenstrual age.

26 - BPD with infection

Code '26' for infants with chronic lung disease requiring respiratory support (nasal cannula, CPAP, or positive-pressure ventilation, either noninvasive or invasive) at 36 weeks' postmenstrual age, who develop a severe intercurrent infection.

27 - BPD with severe CNS insult

Code '27' for infants with chronic lung disease requiring respiratory support (nasal cannula, CPAP, or positive-pressure ventilation, either noninvasive or invasive) at 36

weeks' postmenstrual age and extubated prior to death because of severe brain atrophy, hydrocephalus, etc.

28 – Pulmonary Hypertension (PPHN)

Code '28' for infants with pulmonary hypertension (PPHN) diagnosed clinically or by echocardiography.

29 – BPD with Pulmonary Hypertension (PPHN)

Code '29' for infants with chronic lung disease requiring respiratory support (nasal cannula, CPAP, or positive-pressure ventilation, either noninvasive or invasive) at 36 weeks' postmenstrual age AND with pulmonary hypertension (PPHN) diagnosed clinically or by echocardiography.

Infection**30 - Suspect sepsis/infection**

Code '30' for infants with clinical presentation of septicemia or localized infection without positive cultures during life or on autopsy. The autopsy may reveal polymorph infiltrate of organs and other indications of infection, however cultures are negative.

31 - Proven sepsis/infection

Code '31' for septicemia or localized infection with positive blood or organ cultures. For example, septicemia, meningitis, pulmonary abscess.

GI**40 - NEC**

Code '40' for proven NEC, stage IIA or higher by Bell's criteria as shown in **Appendix G**.

41 - NEC with sepsis

Code '41' for infants with proven NEC (stage IIA or higher by Bell's criteria in **Appendix G**) together with positive blood or peritoneal fluid cultures.

42 - Spontaneous perforation

Code '42' for infants with acute gastrointestinal perforation diagnosed by x-ray without classic radiographic findings of necrotizing enterocolitis or findings of necrotizing enterocolitis at surgery or autopsy, including pathologic specimens.

43 - Short Bowel Syndrome

Code '43' for infants with small bowel resection characterized by malabsorption, diarrhea and failure to thrive.

44 – Liver failure

Code '44' for liver failure if the clinician documents cause of death as liver failure; may include elevated liver enzymes with a presentation of coagulopathy.

CNS insult**50 - Severe intracranial hemorrhage**

Code '50' for infants with severe intracranial hemorrhage (grade III-IV) with a clinical presentation of central nervous system decompensation including seizures, apneas, etc., in the absence of severe respiratory distress syndrome requiring high ventilator settings.

51 - Severe intracranial hemorrhage with infection with culture proven or suspected

Code '51' for infants with severe intracranial hemorrhage (grade III or IV) i.e., documented blood/echodensity/echogenicity in the ventricle with ventriculomegaly and/or blood/echodensity/echogenicity in the parenchyma.

Renal

70 – Renal failure

Code '70' for infants with renal failure noted in the chart as cause of death, characterized by Stage 3 acute kidney injury as described:

Serum Creatinine	Urine Output
SCr rise ≥ 3 X reference SCr * <i>or</i>	<0.3 ml/kg/hour for > 24 hours
SCr ≥ 2.5 mg/dl** <i>or</i>	<i>or</i>
Receipt of dialysis	anuria for > 12 hours

Other

60 – Immaturity without active neonatal treatment

Code '60' should be used for infants receiving no active treatment (i.e. comfort care only) due to extreme prematurity. Infants provided comfort care because of a severe congenital anomaly or other specific cause aside from extreme prematurity should have the specific cause indicated under pre-specified causes listed above. This code should also be used for infants who receive no further active treatment following unsuccessful attempts to resuscitate at birth.

90 - Other

Code '90' for infants with other causes of death such as severe asphyxia with multi-system failure, severe metabolic disease, and severe trauma. Cardiorespiratory arrest is not to be used.

99 - Unknown

Code '99' only if the cause of death has been investigated but could not be established.

Appendix D Retinopathy of Prematurity Diagram

 The image part with relationship ID r1856 was not found in the file.

Appendix E Surgical Procedures

GI – 200 Series	
201	Laparotomy
202	Bowel resection (end to end anastomosis) or repair of perforation
203	Jejunostomy/ileostomy/colostomy—primary surgery or revision
204	Ostomy takedown/reanastomosis
205	Peritoneal drain (used for any reason including NEC or IP)
206	Gastrostomy/G Tube
207	Appendectomy
208	Fundoplication or repair of hiatal hernia
209	T-E fistula/esophageal atresia repair
210	Gastroschisis/omphalocele repair
211	Diaphragmatic hernia repair/hernia of Morgagni
212	Inguinal hernia repair
213	Umbilical hernia repair
214	Open Liver biopsy
215	Strictureplasty
216	Ladd's procedure/malrotation
217	Abdominal wound debridement and closure of abdominal wound/abdomen
218	Pyloromyotomy
219	Anorectoplasty
299	GI other
Pulmonary - 300 Series	
301	Tracheostomy
302	Anterior cricoid split
303	Resection of cystic adenomatoid malformation
304	Bronchoscopy
305	Open lung biopsy
306	Lobectomy
307	Pulmonary sequestration—extralobar
399	Pulmonary other
GU – 400 Series	
401	Repair of extrophy of the bladder
402	Urinary diversion/stent
499	GU other
Head & Neck - 500 Series	
501	Correction of choanal atresia
502	Repair of cleft lip/palate
503	Oral surgical procedure
599	Head & Neck other

CNS – 600 Series	
601	Shunt for hydrocephalus (post hemorrhagic)
602	Shunt for hydrocephalus (not post hemorrhagic)
603	Ventricular reservoir
604	Exteriorization of shunt or shunt revision
605	Shunt removal
606	Repair of meningocele
699	CNS other
Cardiac – 700 Series	
701	Repair of CHD
702	Cardiac shunt procedure
703	PDA Ligation
799	Cardiac other
Other - 900 Series	
901	Central line placement (requiring anesthesia; not including umbilical or percutaneous central lines)
902	Retinal Laser Ablation
903	Scleral Buckle for ROP
904	Vitreectomy for ROP
905	Excision of teratoma
906	Ophthalmology other—not ROP related
999	Other surgeries not listed

Appendix F Data Forms

The following pages contain the data forms for the Survey of Morbidity and Mortality Among Preterm Infants (GDB)

NGO1	SCREENING LOG
NGO2	GENERIC BASELINE FORM
NGO3	GENERIC CLINICAL OUTCOME FORM
NGO3E	GENERIC EARLY DEATH FORM
NGO5	GENERIC LATE CLINICAL OUTCOME FORM
NGO7	GENERIC RESPIRATORY SUPPORT FORM

Appendix G Modified Bell's Staging Criteria for NEC

Stage	Systemic	Intestinal Signs	Radiologic Signs
IA - Suspected NEC	Temperature instability, apnea, bradycardia, lethargy	Elevated pre-gavage residuals, mild abdominal distension, emesis, guaiac positive stool	Normal or intestinal dilation, mild ileus
IB - Suspected NEC	Same as above	Bright red blood from rectum	Same as above
IIA - Definite NEC Moderately ill	Same as above	Same as above, plus absent bowel sounds, ± abdominal tenderness	Intestinal dilation, ileus, pneumatosis intestinalis
IIB - Definite NEC	Same as above, plus mild metabolic acidosis, mild thrombocytopenia	Same as above, plus absent bowel sounds, definite abdominal tenderness, ± abdominal cellulitis or right lower quadrant mass	Same as IIA, plus portal vein gas, ± ascites
IIIA - Advanced NEC Severely ill Bowel intact	Same as IIB, plus hypotension, bradycardia, severe apnea, combined respiratory and metabolic acidosis, disseminated intravascular coagulation, neutropenia	Same as above, plus signs of generalized peritonitis, marked tenderness and distention of abdomen	Same as IIB, plus definite ascites
IIIB - Advanced NEC Severely ill Bowel perforated	Same as IIIA	Same as IIIA	Same as IIB, plus pneumoperitoneum

From: Ped. Clinics of North America, February 1986, Walsh, M., Kliegman, R., Necrotizing enterocolitis: Treatment based staging criteria.

Appendix H Birth Defects Codes

CODE	TYPE OF DEFECT
Central Nervous System Defects - 100 Series	
101	Anencephaly
102	Meningomyelocele
103	Hydranencephaly
104	Congenital Hydrocephalus
105	Holoprosencephaly
199	Other Central Nervous System Defects
Congenital Heart Defects - 200 Series	
201	Truncus Arteriosus
202	Transposition of the Great Vessels
203	Tetralogy of Fallot
204	Single Ventricle
205	Double Outlet Right Ventricle
206	Complete Atrio-Ventricular Canal
207	Pulmonary Atresia
208	Tricuspid Atresia
209	Hypoplastic Left Heart Syndrome
210	Interrupted Aortic Arch
211	Total Anomalous Pulmonary Venous Return
299	Other Congenital Heart Defects
Gastrointestinal Defects - 300 Series	
301	Cleft Palate
302	Tracheo-Esophageal Fistula
303	Esophageal Atresia
304	Duodenal Atresia
305	Jejunal Atresia
306	Ileal Atresia
307	Atresia of large bowel or rectum
308	Imperforate anus
309	Omphalocele
310	Gastroschisis
399	Other Gastrointestinal Defects
Genitourinary Defects - 400 Series	
401	Bilateral Renal Agenesis
402	Bilateral polycystic, multicystic, or dysplastic kidneys
403	Obstructive Uropathy with Congenital Hydronephrosis
404	Exstrophy of the Urinary Bladder
499	Other Genitourinary Defects

Chromosomal Abnormalities – 500 Series	
501	Trisomy 13
502	Trisomy 18
503	Trisomy 21
599	Other Chromosomal Abnormality

Other Birth Defects – 600 Series	
601	Skeletal Dysplasia
602	Congenital Diaphragmatic Hernia
605	Inborn Error of Metabolism (include G6PD)
699	Other Serious and/or Life-Threatening Birth Defect
Pulmonary - 700 Series	
701	Cystic Adenomatoid Malformation (CAM)
799	Other Pulmonary

The following conditions should **NOT** be coded as a Major Birth Defect.

- Extreme Prematurity
- Intrauterine Growth Restriction
- Small Size for Gestational Age
- Fetal Alcohol Syndrome
- Hypothyroidism
- Intrauterine Infection
- Cleft Lip without Cleft Palate
- Club Feet
- Congenital Dislocation of the Hips
- Limb Abnormalities
- Syndactyly
- Hypospadias
- Patent Ductus Arteriosus
- Pulmonary Hypoplasia (use code 401 for bilateral renal agenesis)

Appendix I Clarification of Infection/NEC

BLOOD CULTURE	NEC	ANTIBIOTICS	FINDINGS
Positive	Absent/suspect	≥ 5 days	Late onset sepsis
Positive	Proven	≥ 5 days	NEC and late onset sepsis
Negative	Absent/suspect	≥ 5 days	No LOS, no NEC
Negative	Proven	≥ 5 days	NEC no LOS

Appendix IA

Chorioamnionitis – Pathologic Findings

If “chorioamnionitis” is noted on the placental pathology report or if **any** of the following findings (as defined by the Stillbirth Collaborative Research Network [SCRN] Pathology Protocol) are documented on the placental pathology report, Code YES to histologic chorioamnionitis.

ACUTE CHORIOAMNIONITIS

- Grade I Acute subchorionitis – early acute chorionitis or both. Patchy-diffuse accumulations of neutrophils in the subchorionic plate fibrin and/or membranous chorionic trophoblast layer, (a few scattered neutrophils in the lower ½ of chorionic plate and/or the membranous chorionic connective tissue allowed)
- Grade II More than 10 PMNs per high power field scattered in the chorionic plate or membranous chorionic connective tissue and/or the amnion.
- Grade III Numerous PMNs present without necrosis of the amnion.
- Grade IV Necrotizing chorioamnionitis. Degenerating neutrophils (karyorrhexis), thickened eosinophilic amniotic basement membrane and at least focal amniotic epithelial degeneration/sloughing.

SUBACUTE CHORIOAMNIONITIS

More than occasional mononuclear cells (usually macrophages) in the placental membranes or chorionic plate. Neutrophils may be rare or abundant, but a coexistent acute chorioamnionitis should be present in at least one section. (Mononuclear cells are most frequent near the amnion).

CHRONIC CHORIONITIS

Mononuclear cell infiltrates in chorion without evidence of acute chorioamnionitis.

FUNISITIS

Inflammation of umbilical cord.

VASCULITIS

Inflammation of vessels.

From SCRN Pathology Protocol, Manual of Operations

Appendix J Physiologic Definition of BPD

Purpose

The Physiologic Definition of BPD protocol will be utilized for the infants in the PDA Trial or the BiB Trial. This protocol will allow the definition of BPD to become standardized across network sites.

Objective

To conduct a physiologic monitored reduction of oxygen in eligible infants at 36 +1 weeks corrected age who are receiving oxygen, to establish the definition of bronchopulmonary dysplasia. Infants are screened at exactly 36 weeks of age and if eligible and enrolled in either the PDA Trial or the BiB Trial, receive the challenge as close as possible to 36 weeks but no later than 37 weeks PMA.

Eligibility Criteria

Inclusion Criteria

1. Infants who are part of the Generic Data Base and alive at 36+1 weeks corrected age and enrolled in the PDA Trial or the BiB Trial
2. Supplemental oxygen as follows:
 - A. Infants receiving oxygen by hood at rest^Δ:
 1. Oxygen by hood <27% with majority* of saturations ≥ 90% in prior 24 hours.
 2. Oxygen by hood 27-30% with majority* of saturations ≥ 96% in prior 24 hours
 - B. Infants receiving oxygen by nasal cannula at rest^Δ:
 1. Oxygen by nasal cannula <27% *EFFECTIVE*** oxygen and majority* of saturations ≥ 90% in prior 24 hours.
 2. Oxygen by nasal cannula 27-30% *EFFECTIVE*** oxygen and majority* saturations ≥ 96% in prior 24 hours.
 - C. Infants receiving room air by nasal cannula at ANY liter per minute (lpm) flow.

Exclusion Criteria

1. Need for mechanical ventilation or continuous positive airway pressure (CPAP).
2. Oxygen by hood >30%.
3. Oxygen by nasal cannula >30% *EFFECTIVE*** oxygen.

Please Note:

*Majority defined as ≥90% of saturation readings during the 24 hour time period.

***EFFECTIVE* oxygen applies to infants receiving oxygen via nasal cannula only. *EFFECTIVE* oxygen is determined from *EFFECTIVE FiO₂ CONVERSION TABLES FOR INFANTS ON NASAL CANNULA* which are included.

^ΔSupplemental oxygen requirement is determined at rest. Disregard any temporary increases in O₂ requirement (for desaturation episodes, apnea, bradycardia or procedures when infant returns to baseline in a reasonable amount of time (< 2 hours). Do not include supplemental oxygen given only with feeds.

Methods

Preparation for Oxygen Reduction Challenge

If needed at your institution, permission from parent(s) and/or attending of record will be secured prior to the evaluation.

All infants should be studied in the supine position. Feedings and medications should be given 30 minutes before the evaluation. Bolus feedings should not be given during the evaluation. Infants on continuous feeding may continue feeds during the evaluation.

A pulse oximeter will be placed (if not already in use), the infant positioned and allowed to rest for 5 minutes before baseline readings are started.

Worksheets are provided to document the Oxygen Reduction Challenge for all eligible infants. Results of the challenge will be recorded on the GBD Form NG07.

Oxygen Reduction Phase:

Infants are weaned as follows:

For infants receiving oxygen by hood:

Decrease FiO_2 by 2% every 5 minutes.

For infants receiving oxygen by nasal cannula $\geq 22\%$:

Wean flow in increments of 0.5 lpm every 5 minutes until a flow of 0.5 lpm is reached.

Continue weaning by 0.1 lpm every 5 minutes until a flow of 0.1 lpm is reached.

Continue with Method A or Method B:

Method A - using oxygen blender: with flow at 0.1 lpm, wean FiO_2 by 20% every 5 minutes to room air

Method B - using low flow with 100% oxygen concentration: continue to wean flow every 5 minutes to 0.06 lpm, then 0.03 lpm

For both methods turn off flow, gently remove cannula from nares.

For infants receiving room air by nasal cannula:

If flow > 2 lpm: Wean flow in increments of 2.0 lpm every 5 minutes until a flow of 2 lpm is reached. Continue weaning as below to 0.5 lpm.

If flow 0.5-2.0 lpm: Wean flow in increments of 0.5 lpm every 5 minutes until a flow of 0.5 lpm is reached. Then turn off flow.

If flow is 0.001-0.49 lpm: turn off flow, gently remove cannula from nares.

ALL INFANTS SHOULD:

CONTINUE TO THE NEXT REDUCTION STEP IF SATURATION $\geq 90\%$ DURING THE 5 MINUTE MONITORING PHASE.

STOP REDUCTION IF SATURATION $<90\%$ FOR 5 CONTINUOUS MINUTES OR $<80\%$ FOR 15 SECONDS with good signal fidelity.

Monitoring the oxygen reduction phase:

Document each oxygen reduction step sequentially starting with #1. Use worksheets to record the following.

At each '0' timepoint record:

- a. Starting time
- b. Saturation

- c. FiO_2
- d. If NC, lpm flow

For each minute during the reduction step, record:

- a. Time
- b. Saturation

Continue with reduction steps until the infant is in room air.

Room Air Phase

The infant will be monitored in room air for 30 minutes. If saturations remain $\geq 90\%$ the infant will be considered to have passed the oxygen reduction challenge. The infant should then be placed back in his/her baseline oxygen.

The infant may qualify for a RAPID PASS if all saturations $\geq 96\%$ in room air for 15 consecutive minutes.

If the infant has saturations $<90\%$ for 5 continuous minutes or $<80\%$ for 15 seconds, the infant should be immediately placed back in his/her baseline oxygen. The infant will be considered to have NOT passed the challenge.

Outcome of Challenge

The date and results of the oxygen reduction challenge will be recorded on the NG07 question B.3.

CERTIFICATION

It is important that all personnel performing the oxygen reduction challenge are familiar with patient population and procedures. All personnel are required to read the protocol and review the worksheets used to document the oxygen reduction challenge. It is suggested that a certification exam be employed for personnel. An example of a certification exam follows.

Certification Exam:

Each individual who desires to become certified to perform the Physiologic Evaluation should complete the certification exam to assure familiarity with the methods and evaluation procedures.

CERTIFICATION EXAM

(Duplicate as many as needed for your site before completion)

Name _____ Center _____

1. Consult the Table in the Methods section and indicate whether the following infants should undergo physiologic evaluation for BPD.

A. An infant on a mechanical ventilator	Y	N
B. Infant at 33 weeks gestation	Y	N
C. Infant in room air	Y	N
D. 2.0 kg infant in 2 liters nasal cannula with 100% oxygen, saturation 90 -96%	Y	N
E. 1.8 kg infant in 1.0 liters nasal cannula, 60% oxygen, saturation 90 - 96%	Y	N
F. 1.9 kg infant in 0.25 liters nasal cannula, 70% oxygen, saturation >96%	Y	N
G. 2.1 kg infant in 0.1 liters nasal cannula, and 30% oxygen conc., saturation >96%	Y	N
H. 1.7 kg infant in 0.5 liters nasal cannula, 40% oxygen, saturation >96%	Y	N

2. Determine the final classification (BPD/no BPD) of the following scenarios:

A. Infant has all saturations \geq 96% for 15 minutes in room air	BPD	No BPD
B. Infant has saturation < 90% for 6 minutes	BPD	No BPD
C. Infant has saturation \geq 90% for 30 minutes	BPD	No BPD
D. Infant has most saturation \geq 90%, but has one minute period of saturation of 85% that resolves on its own, and returns to \geq 90%	BPD	No BPD

3. During the physiologic evaluation, the infant has an apnea. What should the researcher do:

- a. Observe the infant without intervention.
- b. Institute the usual routines used in that institution for an apneic infant that generally include increasing levels of support after a brief period of observation to allow the infant to arouse on his/her own.

EFFECTIVE FIO₂ CONVERSION TABLES FOR INFANTS ON NASAL CANNULA.

Tables 1 and 2 allow the determination of the *Effective FiO₂* for infants receiving supplemental oxygen via nasal cannula.

Table 1 identifies a 'factor' by using the infant's current liter flow per minute and the infant's weight. If exact values are not included in the table, round up or down to find the value closest to your patient. If the value is exactly half way in between the two values, then round up.

TABLE 1. FACTOR AS A FUNCTION OF FLOW AND WEIGHT

FLOW (LPM)	FLOW (LPM)	WEIGHT (KG)								
		0.7	1.0	1.25	1.5	2	2.5	3	3.5	4
0.01		1	1	1	1	1	0	0	0	0
0.03	1/32	4	3	2	2	2	1	1	1	1
0.06	1/16	9	6	5	4	3	2	2	2	2
0.125	1/8	18	12	10	8	6	4	4	4	4
0.15		21	15	12	10	8	6	5	4	4
0.25	1/4	36	25	20	17	13	10	8	7	6
0.5	1/2	71	50	40	33	25	20	17	14	13
0.75	3/4	100	75	60	50	38	30	25	21	19
1.0	1.0	100	100	80	67	50	40	33	29	25
1.25		100	100	100	83	63	50	42	36	31
1.5		100	100	100	100	75	60	50	43	38
2.0		100	100	100	100	100	80	67	57	50
3.0		100	100	100	100	100	100	100	86	75
4.0		100	100	100	100	100	100	100	100	100
5.0		100	100	100	100	100	100	100	100	100
6.0		100	100	100	100	100	100	100	100	100

Table 2 determines the *Effective FiO₂* by using the 'factor' and the current oxygen concentration. If exact values are not included in the table, round up or down to find the value closest to your patient. If the value is exactly half way in between the two values, then round up. (See Next page for Table 2)

TABLE 2. EFFECTIVE FiO_2 (x100) AS A FUNCTION OF FACTOR AND CONCENTRATION

FACTOR	CONCENTRATION (%)						
	21	22	25	30	40	50	100
0	21	21	21	21	21	21	21
1	21	21	21	21	21	21	22
2	21	21	21	21	21	22	23
3	21	21	21	21	22	22	23
4	21	21	21	21	22	22	24
5	21	21	21	21	22	22	25
6	21	21	21	22	22	23	26
7	21	21	21	22	22	23	27
8	21	21	21	22	23	23	27
9	21	21	21	22	23	24	28
10	21	21	21	22	23	24	29
11	21	21	21	22	23	24	30
12	21	21	21	22	23	24	30
13	21	21	22	22	23	25	31
14	21	21	22	22	24	25	32
15	21	21	22	22	23	25	33
17	21	21	22	23	24	26	34
18	21	21	22	23	24	26	35
19	21	21	22	23	25	27	36
20	21	21	22	23	25	27	37
21	21	21	22	23	25	27	38
22	21	21	22	23	25	27	38
23	21	21	22	23	25	28	39
25	21	21	22	23	25	28	41
27	21	21	22	23	25	29	42
28	21	21	22	24	26	29	43
29	21	21	22	24	27	29	44
30	21	21	22	24	27	30	45
31	21	21	22	24	27	31	47
33	21	21	22	24	27	31	47
36	21	21	22	24	28	31	49
38	21	21	23	24	28	32	51
40	21	21	23	25	29	33	53
42	21	21	23	25	29	33	54
43	21	21	23	25	29	33	55
44	21	21	23	25	29	34	56
50	21	21	23	25	30	35	60
55	21	22	23	26	31	37	64
57	21	22	23	26	32	38	66
60	21	22	23	26	32	38	68
63	21	22	24	27	33	39	71
67	21	22	24	27	34	40	74
71	21	22	24	27	34	42	77
75	21	22	24	28	35	43	80
80	21	22	24	28	36	44	84
83	21	22	24	28	37	45	87
86	21	22	24	29	37	46	89
100	21	22	25	30	40	50	100

Example:

What is the effective FiO_2 in a 2.0 kg infant on 100% cannula at a flow of 0.15 lpm?

ANSWER: Use 2.0 kg and 0.15 lpm in Table 1 to get a factor of 8. Then use Table 2, and the factor of 8 and 100% oxygen to yield an effective FiO_2 of 27%. Thus the effective oxygen concentration is less than 30% and the infant is eligible for the physiologic evaluation.

PHYSIOLOGIC DEFINITION OF BRONCHOPULMONARY DYSPLASIA WORKSHEET

Date of Oxygen Reduction Challenge ___/___/_____

Network No _____^{BN}

Page 1 of ___

	0 min	1 min	2 min	3 min	4 min	5 min
Baseline (time)	__ : __	__ : __	__ : __	__ : __	__ : __	__ : __
Saturation	_____	_____	_____	_____	_____	_____
FiO ₂	_____	_____	_____	_____	_____	_____
If NC, flow	_____	_____	_____	_____	_____	_____
Reduction step # _____ (time)	__ : __	__ : __	__ : __	__ : __	__ : __	__ : __
Saturation	_____	_____	_____	_____	_____	_____
FiO ₂	_____	_____	_____	_____	_____	_____
If NC, flow	_____	_____	_____	_____	_____	_____
Reduction step # _____ (time)	__ : __	__ : __	__ : __	__ : __	__ : __	__ : __
Saturation	_____	_____	_____	_____	_____	_____
FiO ₂	_____	_____	_____	_____	_____	_____
If NC, flow	_____	_____	_____	_____	_____	_____
Reduction step # _____ (time)	__ : __	__ : __	__ : __	__ : __	__ : __	__ : __
Saturation	_____	_____	_____	_____	_____	_____
FiO ₂	_____	_____	_____	_____	_____	_____
If NC, flow	_____	_____	_____	_____	_____	_____
Reduction step # _____ (time)	__ : __	__ : __	__ : __	__ : __	__ : __	__ : __
Saturation	_____	_____	_____	_____	_____	_____
FiO ₂	_____	_____	_____	_____	_____	_____
If NC, flow	_____	_____	_____	_____	_____	_____

GUIDELINES FOR OXYGEN REDUCTION	WEANING BY HOOD	WEANING BY NASAL CANNULA (NC)			
		Oxygen by nasal cannula <u>≥22%</u>	Method A	Method B	Room Air by nasal cannula
<ul style="list-style-type: none"> Continue to next reduction step if saturations ≥90% Stop reduction if saturation <90% x 5 continuous minutes OR <80% for 15 seconds 	Decrease FiO ₂ by 2% every 5 minutes if saturation ≥90%	<ul style="list-style-type: none"> Wean flow by 0.5 lpm every 5 min until flow of 0.5 lpm reached. Continue wean by 0.1 lpm until flow of 0.1 lpm reached. Continue with either: Method A or Method B 	Using oxygen blender w/ flow at 0.1 lpm: <ul style="list-style-type: none"> Wean FiO₂ by 20% every 5 min to room air. Gently remove cannula Monitor in RA 30 min 	Using low flow w/ 100% O ₂ concentration and flow at 0.1 lpm: <ul style="list-style-type: none"> Continue to wean flow every 5 min to 0.06 lpm then to 0.03 lpm Gently remove cannula Monitor in RA 30 min 	<ul style="list-style-type: none"> Wean flow by 2.0 lpm until flow of 2.0 lpm is reached Wean flow by 0.5 lpm until flow of 0.5 lpm is reached. Gently remove cannula Monitor in RA 30 min

Use as many copies of this form to complete the reduction.

Network No _____

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BN

	0 min	1 min	2 min	3 min	4 min	5 min
Reduction step # _____ (time)	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____
Saturation	_____	_____	_____	_____	_____	_____
FiO ₂	_____	_____	_____	_____	_____	_____
If NC, flow	_____	_____	_____	_____	_____	_____
Reduction step # _____ (time)	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____
Saturation	_____	_____	_____	_____	_____	_____
FiO ₂	_____	_____	_____	_____	_____	_____
If NC, flow	_____	_____	_____	_____	_____	_____
Reduction step # _____ (time)	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____
Saturation	_____	_____	_____	_____	_____	_____
FiO ₂	_____	_____	_____	_____	_____	_____
If NC, flow	_____	_____	_____	_____	_____	_____
Reduction step # _____ (time)	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____
Saturation	_____	_____	_____	_____	_____	_____
FiO ₂	_____	_____	_____	_____	_____	_____
If NC, flow	_____	_____	_____	_____	_____	_____
Reduction step # _____ (time)	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____	____ : ____
Saturation	_____	_____	_____	_____	_____	_____
FiO ₂	_____	_____	_____	_____	_____	_____
If NC, flow	_____	_____	_____	_____	_____	_____

GUIDELINES FOR OXYGEN REDUCTION	WEANING BY HOOD	WEANING BY NASAL CANNULA (NC)			
		<u>Oxygen by nasal cannula</u> ≥22%-	<i>Method A</i>	<i>Method B</i>	Room Air by nasal cannula
<ul style="list-style-type: none"> Continue to next reduction step if saturations ≥90% Stop reduction if saturation <90% x 5 continuous minutes <u>OR</u> <80% for 15 seconds 	Decrease FiO ₂ by 2% every 5 minutes if saturation ≥90%	<ul style="list-style-type: none"> Wean flow by 0.5 lpm every 5 min until flow of 0.5 lpm reached. Continue wean by 0.1 lpm until flow of 0.1 lpm reached. Continue with either: Method A or Method B 	Using oxygen blender w/ flow at 0.1 lpm: <ul style="list-style-type: none"> ◆◆ Wean FiO₂ by 20% every 5 min to room air. ◆◆ Gently remove cannula ◆◆ Monitor in RA 30 min 	Using low flow w/ 100% O ₂ concentration and flow at 0.1 lpm: <ul style="list-style-type: none"> ◆◆ Continue to wean flow every 5 min to 0.06 lpm then to 0.03 lpm ◆◆ Gently remove cannula ◆◆ Monitor in RA 30 min 	<ul style="list-style-type: none"> ◆◆ Wean flow by 2.0 lpm until flow of 2.0 lpm is reached ◆◆ Wean flow by 0.5 lpm until flow of 0.5 lpm is reached. ◆◆ Gently remove cannula ◆◆ Monitor in RA 30 min

ROOM AIR Monitoring

Network No _____
BN

Page ___ of ___

	0 min	1 min	2 min	3 min	4 min	5 min
Time	___:___	___:___	___:___	___:___	___:___	___:___
saturation	_____	_____	_____	_____	_____	_____
Time	6 min	7 min	8 min	9 min	10 min	11 min
saturation	___:___	___:___	___:___	___:___	___:___	___:___
	_____	_____	_____	_____	_____	_____
Time	12 min	13 min	14 min	15 min	16 min	17 min
saturation	___:___	___:___	___:___	___:___	___:___	___:___
	_____	_____	_____	_____	_____	_____
Time	18 min	19 min	20 min	21 min	22 min	23 min
saturation	___:___	___:___	___:___	___:___	___:___	___:___
	_____	_____	_____	_____	_____	_____
Time	24 min	25 min	26 min	27 min	28 min	29 min
saturation	___:___	___:___	___:___	___:___	___:___	___:___
	_____	_____	_____	_____	_____	_____
Time	30 min					
saturation	___:___					

FAIL CRITERIA: Saturation <90% for 5 continuous minutes OR <80% for 15 seconds
RAPID PASS CRITERIA: Saturation ≥96% for 15 consecutive minutes

Appendix K Oral Hypoglycemic Medications

Biguanides

Metformin (Glucophage)
Metformin liquid (Riomet)
Metformin extended release (Glucophage XR, Fortamet, Glumetza)

Sulfonylureas

Glimepiride (Amaryl)
Glyburide (Diabeta, Micronase)
Micronized glyburide (Glynase)

Meglitinides

Repaglinide (Prandin)

D-Phenylalanine Derivatives

Nateglinide (Starlix)

Thiazolidinediones Pioglitazone (TZDs)

Pioglitazone (Actos)

DPP-4 Inhibitors

Sitagliptin (Januvia)
Saxagliptin (Onglyza)
Linagliptin (Tradjenta)

Alpha-glucosidase Inhibitors

Acarbose (Presose)
Miglitol (Glyset)

Bile Acid Sequestrants

Colesevelam (Welchol)

Combination Pills

Pioglitazone & metformin (Actoplus Met)
Glyburide & metformin (Glucovance)
Glipizide & metformin (Metaglip)
Sitagliptin & metformin (Janumet)
Saxagliptin & metformin (Kombiglyze)
Repaglinide & metformin (Prandin)
Pioglitazone & glimepiride (Duetact)

Appendix L Probiotics

Product*	Strain(s)
ABC Dophilus	Bifidobacterium infantis Streptococcus thermophilus Bifidobacterium bifidum
Align	Bifidobacterium infantis
Bios Life Probiotic	Bifidobacterium breve Bifidobacterium lactis Lactobacillus acidophilus Lactobacillus rhamnosus
Culturelle for Kids	Lactobacillus rhamnosus
Culturelle Natural Health and Wellness	Lactobacillus rhamnosus
Discoflor 60	Lactobacillus rhamnosus
UltimateFlora	Bifidobacteria Lactobacilli

*Contact the Data Coordinating Center if a particular probiotic is not listed.

Appendix M

Jensen BPD Criteria

BPD classification based on respiratory support at 36 weeks' postmenstrual age:

BPD grade 0 (no BPD): room air, no respiratory support

BPD grade 1: nasal cannula flow ≤ 2 lpm (regardless of FiO_2)

BPD grade 2: nasal cannula flow > 2 lpm, CPAP, or noninvasive ventilation (regardless of FiO_2)

BPD grade 3: invasive (intubated) respiratory support (regardless of FiO_2 ; includes support via tracheostomy)

Jensen EA et al. *Am J Respir Crit Care Med* 2019;200:751-9