

Pneumonia Etiology Research for Child Health Study - Standard Operating Procedures

This document contains the following standard operating procedures created and used by the Pneumonia Etiology Research for Child Health (PERCH) study investigators.

1. Blood Draw
2. Bronchodilator Challenge
3. 30 Day Follow-Up
4. Case Assessment at 24 and 48 Hours
5. Case Discharge
6. Case Screening and Enrollment
7. Control Enrollment
8. Chest X-Ray
9. Chest X-Ray Online Interpretation
10. Gastric Aspiration
11. Induced Sputum
12. Percutaneous Transthoracic Lung Aspiration
13. Nasopharyngeal and Oropharyngeal Swabs
14. Specimen Collection, Transport, and Storage Algorithm
15. Pleural Fluid
16. Urine Collection
17. Breath Sound Collection
18. PERCH Study ID Scheme
19. Appendix A – PERCH Sample ID Codes
20. Creating Barcode Labels with NiceLabel Software
21. Appendix B – Barcode Labels
22. Creating Barcode Labels with FreezerPro Software
23. Monitoring
24. Regulatory Document
25. SAE Reporting
26. PERCH Organism Dictionary
27. Testing Algorithm
28. Processing of Blood Cultures BACTEC
29. Processing of Blood Cultures BacT/ALERT
30. Antibiotic Susceptibility Testing
31. Bioassay for Detection of Antibiotic Activity in Serum or Urine
32. Quantitative Real-Time *lytA* PCR for *Streptococcus pneumoniae*
33. Nasopharyngeal Culture
34. Processing of Induced Sputum
35. Processing of Pleural Fluids
36. Processing of Lung Aspirate
37. 10A EasyMAG Nucleic Acid Extraction Protocol – Blood Specimens
38. 10B EasyMAG Nucleic Acid Extraction Protocol – Respiratory Specimens

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	► Standard Operating Procedure ◀
Section: Clin Epi	Version: FINAL Initials: ADL
Title: Blood Draw	Revision Date: December 13, 2010

1. Definitions

- 1.1. **Venepuncture** is the term used for the procedure of entering a vein with a needle

2. Purpose / Background

- 2.1. The purpose of this document is to describe the procedures that will be used in the PERCH study for blood collection.
- 2.2. Taking blood samples by finger prick or venepuncture carries a low risk for the patient. However it is a potentially dangerous procedure if not done according to safety standards. Needle stick injuries resulting from improper puncture technique or handling of sharp materials can lead to the transmission of potentially life-threatening infections such as Hepatitis B and HIV. Therefore, it is of utmost importance to adhere to safety principles during the procedure and throughout the process of handling biological samples including proper disposal of clinical/laboratory waste. This includes ensuring that persons involved in blood taking and handling of blood or blood products are vaccinated against Hepatitis B and are wearing gloves whenever samples are obtained or handled.
- 2.3. To minimize the risk of infection of the puncture site and reduce contamination of blood cultures these procedures need to be done under appropriate aseptic conditions, and should only be done after the patient and the parent have been reassured and the patient is as comfortable possible.
- 2.4. The choice of the site for venepuncture should be guided by visibility of superficial veins and understanding of anatomical landmarks so as to avoid any vital structures that may be close to a superficial vein as in appendix. This will minimize the risk of number of attempts at skin puncture and thus discomfort, and also for the purpose of obtaining accurate blood test results.

3. Scope / Applicability

- 3.1. Identify the intended audience and/or areas where SOP may be relevant

4. Prerequisites / Supplies Needed

4.1. Provide Persons taking samples should be trained personnel

- Ensure safety for yourself, patient and others
- Adhere to correct sample taking technique and use correct specimen containers
- Prepare for sample taking
- Sample blood culture first before any other specimen sampling to avoid contamination
- Transfer samples to lab(s) in specified conditions and time span.
- Observe proper disposal of bio-hazard ward, sharps and never re-use sharps_

4.2 Ensure you have all the material that you need BEFORE beginning the procedure:

- 1 pair protective gloves
- 70% alcohol solution
- Appropriate tourniquet

- Butterfly need/appropriate sized needle
- Syringe (5 mL or 10mL)
- Cotton wool swabs
- Sample bottles
- Request forms
- High risk/biohazard specimen labels if required
- Sharps box

5. Roles / Responsibilities

- 5.1. **PERCH Trained Clinicians** will be responsible for taking blood specimens for study/clinical care purposes
- 5.2. **Fieldworkers** will be responsible for taking convalescent sera blood specimens and/or blood specimens from PERCH controls

6. Procedural Steps

6.1. Venepuncture

- 6.1.1. Taking blood from paediatric subjects may be physically traumatic for the infant or child and emotionally traumatic for the mothers. So if sufficient blood is not obtained on the first attempt, a second attempt may be made. If the second attempt also fails, a second person may attempt to obtain the specimen. No more than three attempts should be made for any child at a time. If blood is not obtained after three attempts, the child may be scheduled to return on a later for additional attempts by the most experienced staff member.
- 6.1.2. If three attempts must be made by fieldworker he/she should leave one venepuncture site undisturbed and informs the clinician who will attempt thrice on a peripheral vein if this is not successful, clinician proceeds to a femoral prick.
- 6.1.3. **FEMORAL PRICKS:** only performed by clinicians in older children/adults, femoral area needs very thorough cleaning and sterile gloves are donned before the prick of the vein located medial to the artery.

BLOOD TAKING PROCEDURE

1. Confirm identity of patient
2. Explain the procedure to patient/guardian. Let the patient be on the mother's/guardian's lap or comfortable on an examination coach/bed or seated on a chair. Ask for assistance in restraining a child if necessary BEFORE you begin.
3. Wash your hands thoroughly before the procedure; dry your hands with clean hand towels or gauze.
4. Ensure you have all the equipment that you need. Label containers with patient initials/name, screening/patient number, date, time, ward, type of sample.
5. Arrange specimen containers in the order they will be used.
6. If blood culture is required:
 - a. Ensure that BACTEC bottle is not expired.

- b. Remove the “bottle cap”, clean the rubber top with sterile alcohol swab and allow to dry.
7. Apply the tourniquet on the mid-upper arm or just above the wrist depending on whether you intend to use veins in front of the elbow or back of the hand, respectively.
8. Wear clean gloves.
9. Identify the veins to approach (Appendix 1).
10. Cleanse the area. Use alcohol swabs, cleansing from the venepuncture site outwards, 3 or more times. Allow the alcohol to dry. DO NOT wipe or blow on it to dry. Wash with soap and water if visibly dirty prior to swabbing with alcohol.
11. Assemble venepuncture system using aseptic technique.
12. Perform the venepuncture. Prick the vein gently, if in correct place you will notice a “flash of blood” then slowly pull the syringe plunger to collect specified amount of blood.
13. Release the tourniquet.
14. Collect appropriate volumes of samples in a sterile syringe or by connecting the blood collection tubes to the needle adaptor (volumes are specified in your study/area of work blood sample collection SOP).
15. Withdraw the needle and apply a dry swab. Ask the patient or parent/guardian to hold the swab in place for a few seconds or fold elbow to hold swab in place until bleeding stops usually in a few minutes. If bleeding continues leave swab in place and report to a clinician.
16. If a blood culture is required, place required volume in blood culture bottle first (reduce risk of contamination) before distributing in other bottles. If you are using a scalp needle (butterfly) and syringe, disconnect the butterfly tube and connect a 21-gauge needle to the syringe. Pierce through the rubber top of the culture bottle (cleaned per step 6b) making sure to control the suction effect on the syringe to place required volume.
17. Dispense appropriate volumes to respective tubes. Do not put the syringe down before all the samples have been dispensed and avoid touching the inside of the tubes with the syringe.
18. Make sure the phlebotomist’s initials, date and time of sample collection are marked clearly on the containers and laboratory request form.
19. Dispose of all clinical/laboratory waste into the appropriate containers.
20. Clean the working place, leave clean for next use. Label sample with patient’s name, IP/OPD number, date and time of collection and indicate your initials on the sample collected and the request form.
21. You may need to log in details in a specified log book.
22. Thank parent or guardian for their cooperation.
23. Hand over the samples to the laboratory(s) without delay.

FINGER PRICK FOR CAPILLARY SAMPLE

Ensure that you have all the things that you will need BEFORE beginning the procedure. These are similar to those for blood sample collection but sterile lancets will also be required.

Labelling of slides (site specific?)

Label the slide in pencil on the frosted portion of the slide according to the study protocol involved. Make sure the slide is free from grease and if traces of oil can be observed on the slide.

Preparation of Blood Smears

1. Put on a clean pair of gloves.
2. Clean the middle or ring finger with cotton swab soaked in 70% alcohol.
3. Puncture the ball of the finger with a sterile lancet. **DO NOT REUSE LANCETS!!!**
4. Wipe out the first drop of blood and apply gentle pressure on the finger to release a free flowing drop of blood
5. For the thick smear, collect the drop of blood by touching the drop slightly, controlling the amount of blood to be collected (approx 10-12 ul of blood)
6. Place the slide on the slide template provided and spread the drop using the edge of another clean slide avoiding formation of bubbles.
7. For the thin smear, collect a drop of blood by touching the drop slightly to acquire approx. 2-4 ul of blood.
8. Place the slide on the slide template provided
9. Using a spreader with a smooth edge, touch the drop of blood with the spreader and allow blood to spread along the spreader without touching the edges of the slide.
10. Raise the spreader to an angle of 45° and spread at moderate speed in order to create a feathered edge of the thin smear before reaching the other end of the slide.
11. Protect the smear from flies and dust as you prepare to transport it to the lab.
12. Place the slide flat on the rack provided at the lab reception window accompanied with a well-labelled request form.

Specimen Transport and Storage:

Specimen	Transport/storage conditions*	Until
Blood culture	≤24 h, room temperature or according to manufacturer’s instructions	Placement in blood culture machine
Whole blood (EDTA and plain tubes)	<3 days, 4°C	Specimen separation

7. Record Management

- 7.1. Access, location, and retention of records pertaining to the SOP

8. Quality Assurance / Quality Control

- 8.1. Defines the need, frequency, and methods of conducting QA/QC

8.2. Includes internal and external monitoring

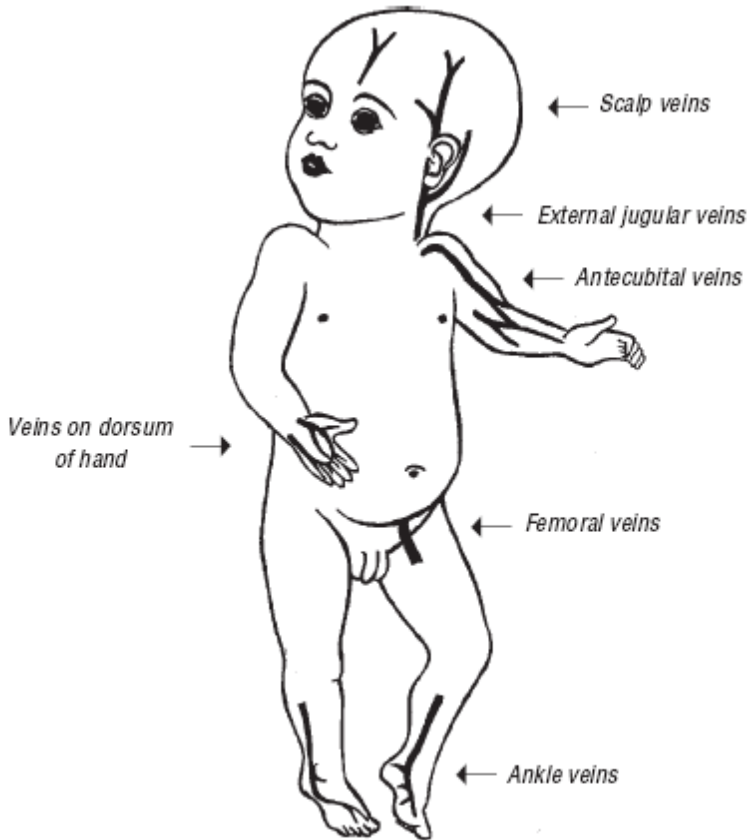
9. References

9.1. Standards: Regulatory references listed

9.2. Other SOPs listed

9.3. Supplementary Documents: Title of any forms used. Do not include actual forms as these may change rapidly which would necessitate a revision in SOP.

APPENDIX I: Sites for intravenous access in infants and young children



Sites for IV access in infants and young children

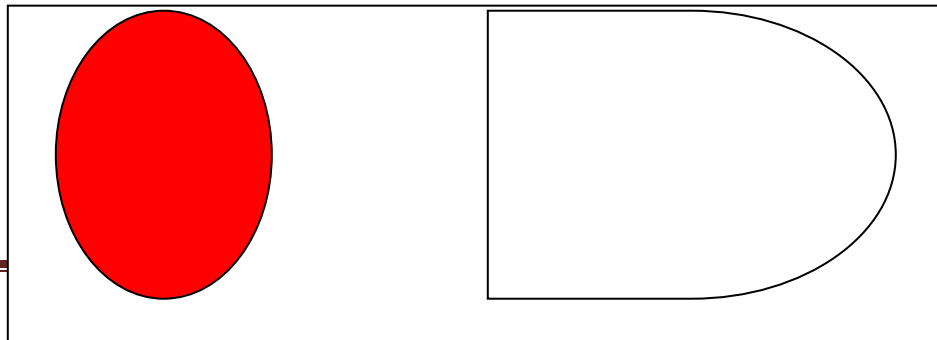
(Source: WHO pocketbook of Hospital Care for Children. World Health Organization 2006.)

APPENDIX II: Example of a thick and thin film smear for malaria diagnosis.

NAME

STUDY
NUMBER

DATE



SOP ID# CE 01
Version: FINAL
Date: 12/13/2010

TIME



► Standard Operating Procedure ◀

Section: Clin Epi

Version: FINAL

Author: D. Feikin

Bronchodilator challenge

Revision Date: December 7, 2010

A. Definitions

- A.1. Bronchodilator is a medicine delivered to the bronchioles to cause them to dilate.
- A.2. “Bronchodilator challenge” refers to a trial of bronchodilators to determine if chest indrawing resolves in children with severe pneumonia. It does not refer to bronchodilators used as treatment for wheezing.
- A.3. “Response” to a bronchodilator challenge means that the physical exam sign of chest indrawing in a child with severe pneumonia resolves after bronchodilation. It does *not* refer to resolution of the wheeze.
- A.3. MDI is a metered-dose inhaler, which refers to application of a bronchodilator by dispensing a fixed amount of medication to a child’s bronchioles, done by depressing a plunger in a small bottle of medicine via a spacer through which the child breathes.
- A.4. Spacer is a short tube used as a conduit between the MDI and the child’s mouth.
- A.5. Nebulizer is a device used to create small droplets of medicine that is breathed in by the child.
- A.6. Wheezing in the context of this SOP refers to both audible and auscultatory wheezing.

B. Purpose / Background

B.1. The purpose of this SOP is to describe standardized approach to the bronchodilator challenge to determine the eligibility of a child with severe pneumonia *and* wheezing into the PERCH study.

B.2. Background: The intent of PERCH is to study children with severe or very severe pneumonia, rather than a study of children with reactive airway disease (RAD). It is well recognized that RAD and pneumonia can co-present in an individual child. However, children with reactive airway disease only (e.g. asthma) can present with clinical findings, such as lower chest wall indrawing, which are essential components of the pneumonia case definition, even though they don’t have pneumonia. We do not want to include as PERCH cases children whose clinical signs, which result in their inclusion as severe or very severe pneumonia cases, resolve in a short period of time following acute therapy with bronchodilators. These children are unlikely to have pneumonia, instead their chest clinical signs are likely attributable to reactive airway disease, an important illness, but not the disease that PERCH is aiming to study. Therefore to differentiate patients whose severe or very severe pneumonia case-defining clinical signs are attributable to reactive airway disease only, we will use an algorithm of response to bronchodilation. The major clinical sign of concern with respect to differentiating RAD from pneumonia is lower chest indrawing. Wheezing patients with very severe pneumonia clinical signs are very unlikely to resolve these signs with bronchodilatory therapy.

B.3. Key principles of the bronchodilator challenge.

B.3.1. Pertains to those with severe pneumonia, not very severe pneumonia (VSP). However, BD can be administered to VSP cases and should be documented but is not required.

B.3.2. Pertains to only those with severe pneumonia *and* wheeze

B.3.3. Pertains to auscultatory wheeze and/or audible wheeze

B.3.4. Response is defined as resolution of chest indrawing, and not resolution of wheeze alone

B.3.5. The bronchodilator challenge can happen before or after PERCH enrollment. This will be determined by each site. For those sites that can do the bronchodilator challenge before enrollment, children who respond to bronchodilation will not be enrolled. For those sites that will do the bronchodilator challenge after enrollment, children who respond to bronchodilation will be entered into a reactive airways disease sub-group, described below in section 1.5.

C. Scope / Applicability

3.1. This SOP is intended for PERCH study staff with a role in enrollment into PERCH.

D. Prerequisites / Supplies Needed (for each participant)

4.1. Stethoscope

4.2. MDI of bronchodilator medicine (or nebulizer)

4.3. Bronchodilator Challenge Worksheet (CRF 01)

E. Roles / Responsibilities

5.1 The bronchodilator challenge will be administered by a PERCH study nurse or clinician.

5.2 A clinician will determine if a case-patient meets criteria for a bronchodilator challenge and what the response is to the bronchodilator challenge.

F. Procedures

1. Determination if a child meets eligibility criteria for a bronchodilator challenge

1.1. Inclusion criteria:

- Severe pneumonia (i.e. chest indrawing present without a danger sign)
- Presence of audible or auscultatory wheeze

1.2. Exclusion criteria:

- Very severe pneumonia (*However, BD can be administered to VSP cases and should be documented but is not required.*)

1.1 If child meets criteria for the bronchodilator challenge, administer two puffs of MDI bronchodilator using a spacer.

1.1.1. While MDI are preferred, if not available then a nebulizer can be used to deliver bronchodilator.

1.2. Wait 15 minutes after bronchodilation and re-assess child.

1.2.1. Evaluate for chest indrawing.

1.2.2. Evaluate for audible and auscultatory wheeze.

1.3. If the chest indrawing has resolved and remains absent for at least 5 minutes, then the child has responded to the bronchodilator challenge. The child should not be enrolled, or if enrolled should be entered into the reactive airways subgroup, as outlined in section 1.5.

1.4. If the chest indrawing has not resolved after the first bronchodilation then do the following:

1.4.1. If the child is < 2 years of age, enroll the child in PERCH without doing further bronchodilation.

1.4.2. If the child is 2-4 years of age, repeat steps 1.1-1.3, up to two more times. If the chest indrawing has not resolved after 3 bronchodilators, enroll the child into PERCH.

1.5. If the chest indrawing did resolve with the bronchodilator challenge, then the child should not be enrolled, or if enrolled should be entered into the reactive airways subgroup, as outlined below:

1.5.1. Children in the reactive airways subgroup:

- Will have collection of: acute blood for culture, HIV testing, CBC, and np/op swabs for PCR.
- Will not have: induced sputum, lung aspirate, urine, or convalescent sera.
- Will not count towards the monthly enrollment of PERCH cases
- Will not contribute to the determination of the number of controls needed in the month.

1.6. Complete the Bronchodilator Challenge Worksheet.



► **Standard Operating Procedure** ◀

Section: Clin Epi

Version: FINAL Author: A. Deluca/ D. Feikin

30-Day Follow Up

Revision Date: December 17, 2010

1. Definitions

1.1. Specific to this SOP

1.1.1. **Vital status** refers to the status of the child at the time of the 30-day follow up visit

1.1.2. **Respiratory rate** is the observed breathing pattern, measured by counting the number of breaths in a full 60 second period

1.1.3. **Oxygen saturation** is the amount of oxygen in the child's blood, measured as a percentage using a pulse oximeter

1.2. Abbreviations

1.2.1. **CO**- clinical officer

2. Purpose / Background

2.1. The purpose of this SOP is to describe the procedures required for case assessment during the follow up visit 30 days after admission to the hospital.

2.2. Background. All patients discharged alive will be followed up 30 days (window 21-90 days) post-admission to assess vital status and to collect a convalescent serum. Ancillary study data or risk factor information will also be collected at this time. CD4 testing will be done on plasma collected from HIV-infected cases in South Africa and Zambia.

2.3. For collection of convalescent sera: Infection can be transmitted from patient to staff and from staff to patient during the blood-taking procedure. Viral agents pose the greatest hazard and in some instances are potentially lethal. Of particular importance are the hepatitis viruses and the human immunodeficiency virus (HIV; the virus causing acquired immunodeficiency syndrome [AIDS]). To decrease the risk of transmission of these viral agents, carefully follow the procedure outlined below for blood collection.

3. Scope / Applicability

3.1. This SOP is intended for clinical staff involved in patient assessment during the 30 day follow up visit.

4. Prerequisites / Supplies Needed

4.1. Scale

4.2. Tape measure (MUAC)

4.3. Respiratory timer

4.4. Pulse oximeter *if available

4.5. Blood collection kit

5. Roles / Responsibilities

5.1. A PERCH-trained CO or physician will perform all physical examinations.

5.2. Study staff may extract information on treatment of wheeze, changes in antibiotics, and other information required for this assessment from the patient's medical record.

6. Procedural Steps

- 6.1. **Vital status (CRF 09, Q2).** Collect information from the interviewee on the status of the child at the time of the interview. If the child has died, complete all of question two, obtaining as much information as possible on date and cause of death.
- 6.2. **Height/weight (CRF 09 Q4 and 5).** Measure the height and weight of the child (*MUAC will be by site*).
- 6.3. **Respiratory Rate (CRF 09, Q7).** Be sure the child is calm. Observe the patient's respiratory rate by watching a chosen location on the child's chest. If the chest is not visible, ask the parents to remove the child's clothing so that you can see his or her torso clearly. Observe the movements as the patient breathes in and out. Set a countdown timer at 60 seconds. Start counting the inward breaths at the same time the counter starts and stop at the end of the 60 seconds when the timer beeps. We are concerned only with the respiratory rate in a calm child as respiratory rate will increase when the child is crying, upset, or actively moving. If you are unsure of the count, repeat this step again. Do not count only 30 seconds and multiply by two as this method may over-estimate the true rate.
- 6.4. **Oxygen saturation (CRF 09, Q8).** Check the patient's blood-oxygen saturation using an age or size appropriate pulse oximeter. Count 4 seconds before recording any reading. Usually, the upper reading appearing on the screen indicates the blood oxygen saturation while the lower reading gives the pulse. Ensure that the pulse is reading on the oximeter to be sure the probe is placed properly and functioning. *It is preferable to measure the child's oxygen saturation on room air, if not clinically contraindicated.* Record the oxygen saturation, noting if the child is breathing with supplementary oxygen or not. If the child has supplemental oxygen, record the rate of oxygen delivery and mechanism of delivery. If it is appropriate include the FiO₂ % oxygen; for example if using a venture mask.
- 6.5. **Collection of Convalescent Sera.** (adapted from WHO manual):
 - 6.5.1. Wear latex or vinyl gloves impermeable to liquids.
 - 6.5.2. Change gloves between patients.
 - 6.5.3. Syringes and needles should be disposed of in a puncture-resistant, autoclavable container. No attempt should be made to recap the needle. A new syringe and needle must be used for each patient.
 - 6.5.4. Wipe the surface of the collection bottle and the gloves with a disinfectant.
 - 6.5.5. Label the bottle.
 - 6.5.6. Specimen containers should be individually and conspicuously labeled. Any containers with blood on the outside should be wiped thoroughly. Such containers should be transported in individual, sealed plastic envelopes.
 - 6.5.7. Remove gloves and discard in an autoclavable container.
 - 6.5.8. Wash hands with soap and water immediately after removing gloves.
 - 6.5.9. Transport the specimen to the microbiology laboratory or, if that facility is closed, store the specimen in an approved location.
 - 6.5.10. In the event of a needle-stick injury or other skin puncture or wound, wash the wound thoroughly with soap and water, encouraging bleeding. Report any contamination of the hands or body with blood, or any puncture wound, or any cut to the supervisor and the health service for treatment, as appropriate.

6.6. Venipuncture

- 6.6.1. Gather everything needed to complete the blood collection process: gloves, syringe, needle, tourniquet, gauze squares, cotton balls, adhesive bandage, puncture resistant container, culture medium and antiseptic; iodine tincture (100 ml of 70% isopropyl alcohol to 1 g of iodine) or povidone-iodine is preferred, but 70% alcohol is an acceptable alternative. The size of the needle will depend on the collection site and the size of the vein. A 23-gauge needle that is 20 – 25 mm in length or a butterfly needle is generally used for children. Collecting a large amount of blood from a child can be difficult: 1 – 3 ml is usually sufficient, but aim to collect 4 mL.
- 6.6.2. Select an arm and apply a tourniquet to restrict the flow of venous blood. The most prominent vein is usually chosen for venipuncture.
- 6.6.3. Vigorously wipe the skin with the 70% alcohol, and swab with the iodine tincture or povidone-iodine. Rub over the selected area. Allow to dry. If the vein is palpated again, repeat the skin disinfection.
- 6.6.4. After the disinfectant has dried, insert the needle into the vein with the bevel of the needle face-up. Once the vein is entered, withdraw the blood by pulling back the barrel of the syringe in a slow, steady manner. Air must not be pumped into a vein. After the desired amount of blood is obtained, release the tourniquet and place a sterile cotton ball over the insertion site while holding the needle in place. Withdraw the needle and have the patient hold the cotton ball firmly in place until the wound has stopped bleeding. Inoculate the culture medium. Put the adhesive bandage on the wound.

7. Record Management

- 7.1. Site Specific

8. Quality Assurance / Quality Control

- 8.1. TBD

9. References

- 9.1. Standards: Regulatory references listed
- 9.2. Other SOPs listed
- 9.3. Supplementary Documents: Title of any forms used. Do not include actual forms as these may change rapidly which would necessitate a revision in SOP.



► **Standard Operating Procedure** ◀

Section: Clin Epi

Version: FINAL

Author: A. DeLuca/ D. Feikin

Case Assessment at 24 and 48 Hours

Revision Date: June 2, 2011

1. Definitions

1.1. Specific to this SOP

- 1.1.1. **Admission** refers to the calendar date of being admitted to hospital (if enrolled after midnight the 24-hour assessment should be performed the following night or the second morning)
- 1.1.2. **Respiratory rate** is the observed breathing pattern, measured by counting the number of breaths in a full 60 second period
- 1.1.3. **Oxygen saturation** is the amount of oxygen in the child's blood, measured as a percentage using a pulse oximeter
- 1.1.4. **Treatment of wheeze** refers to medicines administered to children who present with wheeze after the bronchodilator challenge at the time of enrollment
- 1.1.5. **TB medications** refer to antibiotics administered to TB suspects, and include the following drugs: fixed dose combination TB treatment, INH, ethambutol, rifampin, pyrazinamide, ofloxacin.

1.2. Abbreviations

- 1.2.1. **CO**- clinical officer

2. Purpose / Background

- 2.1. The purpose of this SOP is to describe the procedures required for case assessment at 24 and 48 hours after a child has been admitted to the hospital and enrolled in the study.
- 2.2. Background. Standardized data on a limited set of clinical signs and symptoms (respiratory rate, oxygen saturation and amount of oxygen requirement) will be collected at admission, at 24 and 48 hours after admission to allow inferences to be made about the association between disease progression and specific etiologies and to accurately assess severity. Treatment given during the hospitalization period will also be recorded.

3. Scope / Applicability

- 3.1. This SOP is intended for clinical staff involved in patient assessment at 24 and 48 hours after admission.

4. Prerequisites / Supplies Needed

- 4.1. Respiratory timer
- 4.2. Pulse oximeter
- 4.3. Medical record

5. Roles / Responsibilities

- 5.1. A PERCH-trained nurse, CO or physician will perform all physical examinations.
- 5.2. Study staff may extract information on treatment of wheeze, changes in antibiotics, and other information required for this assessment from the patient's medical record.

6. Procedural Steps

- 6.1. **Respiratory Rate** Be sure the child is calm. Observe the patient's respiratory rate by watching a chosen location on the child's chest. If the chest is not visible, ask the parents to remove the child's clothing so that you can see his or her torso clearly. Observe the movements as the patient breathes in and out. Set a countdown timer at 60 seconds. Start counting the inward breaths at the same time the counter starts and stop at the end of the 60 seconds when the timer beeps. We are concerned only with the respiratory rate in a calm child as respiratory rate will increase when the child is crying, upset, or actively moving. If you are unsure of the count, repeat this step again. Do not count only 30 seconds and multiply by two as this method may over-estimate the true rate.
- 6.2. **Oxygen** If the child has supplemental oxygen, record the rate of oxygen delivery and mechanism of delivery.
- 6.3. **Oxygen saturation** Check the patient's blood-oxygen saturation using an age or size appropriate pulse oximeter. Count 4 seconds before recording any reading. Usually, the upper reading appearing on the screen indicates the blood oxygen saturation while the lower reading gives the pulse. Ensure that the pulse is reading on the oximeter to be sure the probe is placed properly and functioning. *It is preferable to measure the child's oxygen saturation on room air, if not clinically contraindicated.* **Medical record abstraction.** Review the child's medical record to determine if any of the following were done since the time of admission and enrollment:
- 6.3.1. **Wheeze.** The child has been treated for wheeze *after* the bronchodilator challenge that was administered as part of enrollment.
- 6.3.2. **Change in antibiotics.** The child had a change in their antibiotic treatment regimen since the last assessment. For the 24 hour assessment, this will be since admission. For the 48 hour assessment, this will be since the 24 hour assessment. If antibiotics have changed, note the reason for change in antibiotics, including not responding to initial therapy.
- 6.3.3. **PCP Medications.** The child has been started on a treatment regimen for PCP. Note the medication used and the reason it was started.
- 6.3.4. **TB Medications.** The child has been started on a treatment regimen for suspected/confirmed tuberculosis. Note the reason for starting treatment.
- 6.3.5..
- Clinical Status.** Record any of the WHO severe pneumonia danger signs, and describe their WHO pneumonia severity classification.

7. Record Management

- 7.1. Site Specific

8. Quality Assurance / Quality Control

- 8.1. TBD

9. References

- 9.1. Standards: Regulatory references listed
- 9.2. Other SOPs listed

9.3. Supplementary Documents: Title of any forms used. Do not include actual forms as these may change rapidly which would necessitate a revision in SOP.



► **Standard Operating Procedure** ◀

Section: Clin Epi

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Author: A. DeLuca/D. Feikin

Case Discharge

Revision Date: December 17, 2010

1. Definitions

1.1. Specific to this SOP

1.1.1. **Respiratory rate** is the observed breathing pattern, measured by counting the number of breaths in a full 60 second period

1.1.2. **Oxygen saturation** is the amount of oxygen in the child's blood, measured as a percentage using a pulse oximeter

1.1.3. **Discharged home with persistent abnormality** is an ongoing clinical abnormality related to the pneumonia episode. This might include altered level of consciousness due to hypoxia, complications of an associated meningitis, such as hearing loss, or ongoing, new bronchospasm requiring treatment.

1.2. Abbreviations

1.2.1. **CO**- clinical officer

2. Purpose / Background

2.1. The purpose of this SOP is to describe the procedures required for case discharge.

2.2. Background. Standardized data on a limited set of clinical signs and symptoms (respiratory rate, oxygen saturation) will be collected at discharge to allow inferences to be made about the association between disease progression and specific etiologies and to accurately assess severity. Discharge diagnosis and clinical status will also be evaluated (i.e., whether fully recovered, left against medical advice, died, etc.).

3. Scope / Applicability

3.1. This SOP is intended for clinical staff involved in patient discharge.

4. Prerequisites / Supplies Needed

4.1. Respiratory timer

4.2. Pulse oximeter

4.3. Medical record

5. Roles / Responsibilities

5.1. A PERCH-trained CO or physician will perform all physical examinations.

5.2. Study staff may extract information on treatment of wheeze, changes in antibiotics, and other information required for this assessment from the patient's medical record.

6. Procedural Steps

6.1. **Respiratory Rate (CRF 08, Q4)**. Be sure the child is calm. Observe the patients respiratory rate by watching a chosen location on the child's chest. If the chest is not visible, ask the parents to remove the child's clothing so that you can see his or her torso clearly. Observe the movements as the patient breathes in and out. Set a

countdown timer at 60 seconds. Start counting the inward breaths at the same time the counter starts and stop at the end of the 60 seconds when the timer beeps. We are concerned only with the respiratory rate in a calm child as respiratory rate will increase when the child is crying, upset, or actively moving. If you are unsure of the count, repeat this step again. Do not count only 30 seconds and multiply by two as this method may over estimate the true rate.

- 6.2. **Oxygen saturation (CRF 08, Q5).** Check the patient's blood-oxygen saturation using an age or size appropriate pulse oximeter. Count 4 seconds before recording any reading. Usually, the upper reading appearing on the screen indicates the blood oxygen saturation while the lower reading gives the pulse. Ensure that the pulse is reading on the oximeter to be sure the probe is placed properly and functioning. It is preferable to measure oxygen saturation on room air if clinically indicated. Record the oxygen saturation noting if the child is breathing with supplementary oxygen or not.
- 6.3. **Medical record abstraction.** Review the child's medical record to determine the following:
 - 6.3.1. **Respiratory procedures done during hospitalization (CRF08, Q6).** Record all procedures that were done during hospitalization according to the checklist.
 - 6.3.2. **Clinically significant events during hospitalization (CRF08, Q7).** Record all events considered 'clinically significant' according to the checklist.
 - 6.3.3. **Change in antibiotics (CRF 08, Q8).** The child had a change in their antibiotic treatment regimen since the last assessment. If antibiotics have changed, note the reason for change in antibiotics, including not responding to initial therapy.
 - 6.3.4. **TB Medications (CRF 08, Q9).** The child has been started on a treatment regimen for suspected/confirmed tuberculosis. Note the time of administration.
 - 6.3.5. **Discharge diagnosis (CRF 08, Q10).** Record if the child was discharged due of the reasons listed, and record any concurrent conditions as listed.
 - 6.3.6. **Date and time of discharge/transfer/death.** Note the reason, time, and date for any of these events.

7. Record Management

- 7.1. Site Specific

8. Quality Assurance / Quality Control

- 8.1. TBD

9. References

- 9.1. Standards: Regulatory references listed
- 9.2. Other SOPs listed
- 9.3. Supplementary Documents: Title of any forms used. Do not include actual forms as these may change rapidly which would necessitate a revision in SOP.

	► Standard Operating Procedure ◀
Section: Clin Epi	Version: FINAL Initials: MDK
Title: Case Screening and Enrollment	Revision Date: Aug 4, 2011

1. Definitions and abbreviations

1.1. definitions

- 1.1.1. Severe pneumonia - cough or difficulty breathing AND lower chest wall indrawing
- 1.1.2. Very severe pneumonia - cough or difficulty breathing AND having one or more of the following signs or symptoms: Head nodding, central cyanosis, unable to feed, vomiting everything, lethargy or impaired consciousness, or multiple (≥ 2 within a 24 hour period) (or prolonged (≥ 15 minutes) convulsion(s)
- 1.1.3. Modified protocol - a reactive airways subgroup for children whose case-defining signs of severe pneumonia resolved upon administration of bronchodilator therapy. These cases will have collection of acute blood for culture, HIV testing, CBC, and NL/OP swabs for PCR. They will not have induced sputum, lung aspirate, urine, or convalescent sera collected. They will not count towards the monthly enrollment of PERCH cases and will not contribute to the determination of the number of controls needed in the month.
- 1.1.4. Catchment area – pre-defined geographic area serving the hospital in which cases and controls must reside in order to be eligible for enrollment.
- 1.1.5. Prior hospitalization – admission for at overnight for any reason during the 14 days prior to presentation at the Study Hospital. Includes hospitalization at the referral hospital. Trained examiner - PERCH study personnel (at most sites a physician) trained by Jane Crawley in standardized assessment of case-defining signs and symptoms.
- 1.1.6. Bronchodilator challenge – administration of at least 1 dose of bronchodilator therapy either pre- or post-enrolment in children < 2 years, or at least 3 doses either pre- or post-enrolment in children 2- < 5 years to children meeting the definition for severe pneumonia but not very severe pneumonia and who have wheeze.

1.2. Abbreviations

- 1.2.1. ER: emergency room
- 1.2.2. ICU: intensive care unit
- 1.2.3. CRF: case report form

2. Purpose / Background

- 2.1. The purpose of this SOP is to describe standardized approach to screening to determine the eligibility of a child for enrolment into the PERCH study.

3. Scope / Applicability

- 3.1. This SOP is intended for PERCH study staff with a role in screening and enrollment into PERCH.

4. Prerequisites / Supplies Needed

- 4.1. CRF 01 Case Screening and Enrolment Form

- 4.2 CRF 02 Bronchodilator Challenge Worksheet
- 4.3 Stethoscope
- 4.4 site specific geographic coding list of residence

5. Roles / Responsibilities

- 5.1. Screening nurse – (1) screens for objective eligibility criteria such as age, residence within the catchment area, previous hospitalizations, etc., (2) assessment of cough/difficulty breathing, (3) conducts informed consent procedures.
- 5.2. Trained examiner – confirms presence of standardized case-defining signs and symptoms of severe and very severe pneumonia, performs Bronchodilator Challenge and assesses persistence of lower chest wall indrawing. *Sites to describe if nurse or physician.*
- 5.3. Supervisor – reviews the CRF for proper completion, makes note of any anomalies or problems encountered.

6. Procedural Steps

- 6.1. Selection of cases – *sites to describe any selection process they are using to restrict the number of cases enrolled, such as enrolling every other day.*
- 6.2. Identification of cases: *[Sites to describe how and where potential cases are first encountered, evaluated and logged in at the hospital. For example: Children coming to the hospital will present to the triage desk where they are seen by a hospital nurse and logged into the Hospital Visit Log Book (this is a hospital log, not a study log, that notes the child's name, DOB, date presented, time presented, chief presenting diagnosis/complaint, and where directed to go next). Children with cough or difficulty breathing will be directed by hospital staff to be seen by the PERCH Study Nurse (or PERCH nurse checks hospital log books to look for potential cases).]*
- 6.3. Assigning PERCH Study ID number: The PERCH Study Nurse logs the potential case into the Screening Log Book, recording the name of child and assigning their Screening ID Number by selecting the next available sheet of Study ID labels and affixing one label to the Screening Log. *[Sites to describe location, study staff involved and process to identify which patients to screen].*
- 6.4. Timing with respect to administration of antibiotics: potential PERCH cases must be identified as soon as possible after presenting to the hospital and before antibiotics are administered at the study hospital. Cases who have received antibiotics at the study hospital prior to enrollment are still eligible if blood cultures were collected prior to administration of antibiotics.. *Sites to describe relative timing of screening wrt admission status: if prior to /during /after admission.*
- 6.5. The Screening nurse assesses the non-clinical eligibility criteria listed in Section A of CRF01.
 - 6.5.1. All children of eligible age (≥ 28 days to 59 months) with cough or difficulty breathing should be assessed for PERCH eligibility by the Screening Nurse.
 - 1. Note that the age criteria are inclusive, and no age adjustments should be made to account for prematurity.
 - 6.5.2. The screening nurse must answer all questions in this Section, unless one of the inclusion or exclusion criteria are not met (implying “not eligible”), in which case the.
 - 6.5.3. If the child was deemed not eligible in Section A, the partially completed CRF must be retained and entered into the database.

6.5.4. Inclusion criteria:

- **Age in months.** Record the age in months, or days if less than one month, for all screened children.

For all children >1 month old, do not round the age, but instead record the age achieved. For example, if the child is 3 months and 25 days, record '03' months.

Age is required for all eligible children, whether or not they enroll, so that the representativeness of those enrolled can be compared to those who did not.

Because PERCH requires date of birth (DOB) only for enrolled children, DOB is collected at the end of the screening and enrollment process.

- **History of cough or difficulty breathing:** direct observation by the nurse/physician is not required and may be determined by parental report. Children with chronic lung or respiratory disease are eligible to participate in the study. Since the duration of the history of symptoms is unlikely to be reliable or precise, we will not exclude patients from the study on the basis of a long history of symptoms, but will solicit this information and examine the effect of illness duration on the spectrum of pathogens in post hoc sub-category analyses. NOTE: if child's difficulty breathing is due to **paraffin ingestion**, this child will be included. Sites should gather information on how many of their cases are presenting with or cough or difficulty breathing and report of paraffin ingestion, and we will reassess this inclusion criteria no more than six months in to the study.
- **Residence within the catchment area.** Ask the exact address of where the child usually lives and code using site specific geographic coding list [*sites to create*]. Note that the residence may not always be the address where the child was staying when they became ill (e.g., in the last month), such as if they were recently visiting their grandparent's village outside the catchment area. These children will still be eligible. However, children who usually live outside the catchment area but were visiting the catchment area when they became ill are not eligible. Plans to reside outside the catchment area after discharge will not affect the child's eligibility status.

6.5.5. Exclusion Criteria

- **The child has not been hospitalized for any cause within the last 14 days.** "Hospitalized" is defined as any hospitalization longer than over night within the past fourteen days. We anticipate that many patients will be referred from other hospitals, which is acceptable, and they may be included in PERCH if they were not admitted there. This criterion is meant to exclude children (1) whose clinical signs and symptoms cannot be described at presentation and (2) whose specimens may have been contaminated with nosocomial organisms.

- **If the child was previously enrolled as a PERCH case, at least 30 days have passed from the date of hospital discharge for that pneumonia episode.** A child may be a ‘case’ more than once, but only if the hospitalizations are separated by at least 30 days to ensure the same episode is not captured more than once. If a child was discharged from hospital <30 days and had severe or very severe pneumonia, but was NOT enrolled in PERCH, they should be considered as eligible, so long as they have not been hospitalized longer than overnight in the past 14 days.

6.5.6. **Demographic and risk factor evaluation:** If the child meets the above eligibility requirements, the screening nurse then completes the demographic and risk factor section at the end of Section A of CRF 01. This information should be asked of all children eligible for PERCH, even those who decline participation or are not enrolled for other reasons.

- **HIV status:** HIV status can be determined from verbal report from mother/caregiver or from medical records if available. Mention or documentation/evidence that the child has taken ART medications is sufficient to record “yes” (child is HIV positive). Note: if the child’s caregiver chooses not to provide this information, this will not affect the child’s eligibility status and they may still be enrolled.
- **Sickle cell disease:** Determine from verbal report from mother/caregiver or from medical records if available. If the parent refuses to answer whether or not the child has SCD, this will not affect the child’s eligibility status.

6.6. **Is the child being treated with oxygen?** This is an indication of the severity level of the child at presentation and will be used to assess the representativeness of children enrolled compared to those not enrolled. If the child was observed to have received oxygen at the study hospital at any time before completion of the screening and enrollment process, check “yes”. In some instances, the child may be started on oxygen therapy after the nurse screening assessment, but before consenting process, such as during the examiner’s evaluation. In such a case, an initial recording of “no” must be changed to “yes”. **If the child meets the above eligibility and exclusion criteria,** the screening nurse then refers the child to the trained examiner (at most sites this is a physician) for confirmation that the child meets the PERCH definition for severe or very severe pneumonia (Section B of CRF 01).

6.6.1. If the child was potentially eligible but could not or was not evaluated by the PERCH trained examiner, the reason why must be stated. For example, in some cases the child might be so severely ill that the child dies before the examiner has an opportunity to assess the child’s case-defining symptoms. Or a parent may refuse to be assessed or answer any more questions (i.e., refuses to participate in PERCH).

6.6.2. Record the physical location within the hospital of where the trained examiner assessed the child. In some instances, an atypical location may result in (and can explain) anomalies found despite following a consistent, standardized study protocol. For example, at a site where most cases are evaluated at the admission ward, occasionally a very severely ill child may be sent directly to the

ICU. Because limited PERCH staff cannot be two places at once, it may be that a child sent to the ICU is not evaluated as quickly, which may help to explain out-of-order procedures, such as administration of antibiotics prior to completion of screening and enrollment of the child.

- 6.6.3. The trained examiner assesses the child for presence of all case-defining severe and very severe pneumonia signs and symptoms as trained by Jane Crawley using standardized criteria that will be employed at all sites. To be eligible, the child must have at least one of the shaded boxes in Q12.a to 12.g ticked “yes”. If all are ticked “No”, the child does not meet the PERCH case-defining signs of severe pneumonia or very severe pneumonia and is not eligible. The examiner must check “yes” or “no” for each sign/symptom and should continue to check all remaining symptoms even after a “yes” has been determined for one of the signs/symptoms. This is because this is the only place these signs/symptoms will be recorded (i.e., they are not assessed again later during the Case Clinical Assessment) and they will be used to further characterize the cases.
- “Yes” may be checked for the following signs and symptoms if present on examination by the trained examiner OR if the parent reports a history of the sign/symptom associated with this illness that in the opinion of the trained examiner is consistent with the standardized definition:
 - Lower chest wall indrawing
 - Head nodding
 - Central cyanosis
 - A single prolonged convulsions (≥15 minutes) or multiple convulsions (≥2 within a 24 hour period in the current illness) during this current illness
 - The following signs and symptoms must be observed on examination by the trained examiner:
 - Unable to feed
 - Vomiting everything
 - Lethargy or impaired consciousness. The AVPU score is used to assess “Lethargy or impaired consciousness”. NOTE that if the child is having convulsions, wait for at least 30 minutes after any convulsion before carrying out assessment of consciousness level.
 - If the child is having convulsions, Q12.f. “Lethargy or impaired consciousness” can be temporarily skipped until the AVPU score can be assessed. The screening procedures can progress, including enrollment (since the child has convulsions, if the child meets the definition for very severe pneumonia and can be enrolled if all other criteria are met). In such a case, “Lethargy or impaired consciousness” should be assessed as soon as 30 minutes has passed since the convulsion, and question Q12.f. on CRF01 must be updated at that time.
- 6.6.4. Cases who do not meet the definition for severe or very severe pneumonia at the time of admission but who later progress to severe pneumonia during

hospitalization are not eligible. This is for two reasons: 1) recruiting patients at a fixed point, admission, is considerably simpler and less expensive than establishing continuous recruitment of inpatients, 2) the project aims to define etiology to support prescribing policy for children “on admission” and cases that progress in severity after admission would not contribute to this process, and 3) assessment of etiology may be complicated by nosocomial infections.

6.7. If the child has lower chest wall indrawing and does not meet any of the criteria for “very severe pneumonia”, the examiner must then assess if the child’s lower chest wall indrawing is due to reactive airway disease and not pneumonia (see Bronchodilator Challenge SOP).

6.7.1. All children who meet the case definition of very severe pneumonia will be recruited into the PERCH study regardless of their wheezing status or response to bronchodilator therapy. However, if a child with very severe pneumonia and wheeze can receive bronchodilator therapy (if so, record whether any lower chest wall indrawing resolves following bronchodilator therapy on the Bronchodilator Challenge Worksheet CRF02). It is important to note that the bronchodilator challenge is NOT required for any child with very severe pneumonia.

6.7.2. Ideally the bronchodilator challenge would take place immediately and an assessment of whether the child’s illness meets the severe pneumonia case definition would follow that acute therapy. However, for PERCH we also want to assure that respiratory specimens are collected prior to antibiotic administration. If enrollment in PERCH must await the response to bronchodilation, and if antibiotic administration must await a decision regarding PERCH enrollment and specimen collection, it is possible this sequential approach could delay the receipt of antibiotics for some children at some sites. The PERCH study should not create an impediment or delay in delivering essential clinical management for children with respiratory illness. In such a case, these children may be enrolled into PERCH allowing for the immediate collection of diagnostic specimens. If their case-defining signs of severe pneumonia resolve following bronchodilator challenge, they will remain in the PERCH study but will follow a modified version of the protocol and certain specimens will not be collected.

6.8. If the child meets the above clinical eligibility criteria, the hospital admission status is then confirmed. Because PERCH is a study of severe hospitalized pneumonia, only children referred for admission by hospital physicians (or deemed severe enough for admission by study a physician) are eligible. If the child was referred for admission but the parent refuses, the child can still be enrolled if parents agree to allow the child to remain in hospital long enough for all study specimens to be collected, and to bring the child back daily to assess the child’s status and outcome.

6.9. Final eligibility determination should be determined by the trained clinician, and not the screening nurse.

6.10. Eligible cases are referred to the Screening Nurse to obtain Informed Consent (see Informed Consent SOP).

- 6.10.1. After Informed Consent is obtained, the child's date of birth and the date and time consent was obtained is recorded. The date/time of consent will be considered the date/time the case was enrolled in PERCH.
- 6.10.2. If consent is not obtained, please mark the reason why not.
- 6.10.3. Once enrolled, the sheet of Study ID labels will be used to label any paper CRFs or logs pertaining to this case.

6.11. Screening CRFs for non-enrolled patients WILL be labeled; any remaining labels can be discarded.

6.12. If the child is subsequently found to be ineligible after enrolment (i.e., if child was subsequently discovered to have been hospitalized in the past 14 days), the child will be excluded at that time and no further study evaluation will be performed.

7. Record Management

7.1. Access, location, and retention of records pertaining to the SOP: *sites to describe*

8. Quality Assurance / Quality Control

8.1. *Sites to define the frequency and methods of conducting QA/QC*

8.2. External monitoring: (see clinical monitoring plan)

9. References


9.1. Bronchodilator Challenge SOP

9.2. Informed Consent SOP

9.3. Case Screening and eligibility CRF 01

9.4. Bronchodilator Challenge Worksheet CRF 02

9.5. clinical monitoring plan

	<p>► Standard Operating Procedure ◀</p>
<p>Section: Clin Epi</p>	<p>Version: FINAL Author: D. Feikin</p>
<p>Control Enrollment</p>	<p>Revision Date: December 5, 2010</p>

1. Definitions

- 1.1. Control – A child without severe/very severe pneumonia.
- 1.2. Active control list – selected controls on monthly list to be enrolled
- 1.3. Backup control list – selected controls on monthly list not initially to be enrolled, but only if needed
- 1.4. Demographic Surveillance System
- 1.5. Control Screening and Enrollment Logs – identifies the child to be enrolled; documents whether the child was located, eligibility status, willingness to participate; and schedules interview and specimen collection

2. Purpose / Background

- 2.1. The purpose of this SOP is to describe standardized approach to selection and enrollment of controls at all PERCH sites.
- 2.2. Controls will be selected from the community from which the cases are coming (but not matched by geographic location). Approximately 1 control per case will be enrolled. PERCH sites will recruit a minimum of 25 controls per month. In months where the number of cases exceeds 25, sites will enroll additional controls to achieve a 1:1: ratio (i.e., the same number) as cases enrolled that month.

3. Scope / Applicability

- 3.1. This SOP is intended for PERCH study staff with a role in selection and/or enrollment of controls.

4. Prerequisites / Supplies Needed (for each participant)

- 4.1. Data manager. Computer program for random selection
- 4.2. Data manager. A summary of the number of cases enrolled to date by week.
- 4.3. Field/clinic. Control Screening and Enrollment Logs to identify children selected for control enrollment and log enrollment status
- 4.4. Field/clinic. CRFs: Form 1A: Community Control Screening and Enrolment Form
 - Form 2: demographics
 - Form 3: clinical history
 - Form 4A: clinical assessment
 - Form XX-XX: Control specimen collection forms
- 4.5. Field/clinic. Thermometer
- 4.6. Field/clinic. Stopwatch

5. Roles / Responsibilities

- 5.1 A data manager will randomly identify controls to be enrolled.
- 5.2 A field supervisor will assign field workers to interview and evaluate the identified controls.
- 5.3 Field workers will interview and evaluate eligibility of identified controls.

- 5.4 Trained clinical study personnel will enroll eligible controls , complete all clinical and demographic assessments, and collect specimens. Depending on the site, controls may be enrolled and assessed either in the field or in the clinic.

Procedures

1. Selection of monthly controls from catchment area

1.1. Selection of controls in sites with a DSS (Gambia, Kilifi, Bangladesh) or a birth registry (South Africa)

1.1.1. Determine the annual percentage of severe/very severe pneumonia cases in the following age groups: 28 days-5 months, 6-11 months, 12-23 months, and 24-59 months. (The previous calendar year's data can be used to do this.)

1.1.2. Generate the monthly random control selection list. Using the DSS/birth registry database of children, randomly select approximately 50-100* children 0**-59 months of age using the probability distribution of cases in the four age groups*** – 28 days-5 months, 6-11 months, 12-23 months, and 24-59 months – as determined in step 1.1.1. These ~50-100 children should be arranged in a numbered list in the order in which they were randomly selected. The randomization list for controls to be enrolled in the upcoming month should be generated <1 week before the start of that month and should use the most up to date DSS/birth registry updated to include births >=2 weeks ago.

*The number of controls needed on the monthly random selection list will differ by site and will depend on the projected number of cases to be enrolled for that month (whether if >25 or not) and on the control consent rates. The list includes the number of projects number of controls needed for that month, plus be a back-up list of children to be enrolled if some children among the first 25 are not enrolled, or if it is a month when >25 cases are enrolled. For example, if a site projects fewer than 25 cases will be enrolled in the upcoming month and anticipates 75% of controls will consent to participate, then the list could contain at least 35 controls (approximately 25/.75). If a site projects 50 cases will be enrolled in the upcoming month and anticipates 75% of controls will consent to participate, then the list should contain at least 70 controls (approximately 50/.75). If sites prefer to generate monthly lists of fixed sizes (i.e., the same size for every month) for ease in programming and logistics, N=100 is suggested to accommodate participation refusal rates and months where the number of cases (and thus controls) will exceed N=25.

**Children < 28 days need to be included in this random list because they will become age-eligible in the following month. (See section 2.3)

***Cumulatively over the course of the PERCH project, the age distribution of the controls should match that of the cases. The monthly random control selection list nor the controls actually enrolled per month need to *exactly* match either the projected case age distribution or the actual case age distribution for that month. I.e, there will be randomness in the month-to-month age distribution that will produce short-term imbalances, but these should even out over time. See Section 1.1.5.6 on re-generating the age distribution probabilities.

1.1.2.1. If the random control selection list is exhausted before the required number of controls for that month are enrolled, a supplemental randomization must be generated.

1.1.2.2. Initially, the first 25 children on the list will be considered as the “active control list” and children #26-100 will be considered as the “backup control list.”

1.1.3. Assign specific controls from the active control list to each field worker. SITES SHOULD SPECIFY HOW THEY WILL DIVIDE UP THE CONTROLS BETWEEN FIELD WORKER TEAMS HERE.

1.1.4 Create “Control Screening and Enrollment Logs” for each field worker. Enter the assigned controls from the Active Control List onto a Control Screening and Enrollment Log that will document the status of the following: finding the parent and child, determining eligibility, assessing willingness to participate, scheduling interview and specimen collection.

1.1.5. Order of control enrollment (First 25 controls, Field team).

1.1.5.1 Only children on the “Active Control List” can be approached for enrollment. Initially, only the first 25 children on the control list serve as the “Active Control List”. Only if (a) >25 cases are enrolled that month, or (b) one of the 25 controls on the Active Control List is deemed either “ineligible”, “died”, “out-migrated”, “not at home after at least 2 visits on different days”, or “does not consent” should the “backup control list” be used (i.e. the 26th child be approached for enrollment).

1.1.5.2 Within the Active Control List, the order in which children are enrolled in a calendar month is flexible. For example, if three children on that list (e.g. # 3, 16, 20) live in the same village, they can be enrolled on the same day and others (e.g. #1, 8, 25) can be enrolled on a separate day. However, children on the backup list should not be enrolled, even if living in the same village as children on the eligible list, until those children become eligible for enrollment.

1.1.5.3 The first 25 controls do not have to be evenly enrolled throughout the month. For example, they can be enrolled in the first two weeks of the month.

1.1.5.4. There will be children on the Active Control List who are < 28 days of age at the start of the month. Their visits should be timed when they are \geq 28 days of age. Similarly, for children who will have their 5th birthday that month, their visit should be timed before they turn 5 years of age.

1.1.5.5. Children from the backup list should be moved to the Active Control List in sequential order by age strata. This means that the backup list should be grouped by the following age strata:

- 28 days – 5 months
- 6 – 11 months
- 12 – 23 months
- 24 – 29 months

1.1.5.6 Regenerating age distribution probabilities should be done every month and back up lists should be organized every month by age strata.

1.1.6. Extra control enrollment beyond 25 controls (Field). If an excess of 25 cases are enrolled in a month, then extra controls will need to be enrolled to have the same number as cases.

1.1.6.1 There are three possible ways to determine if more than 25 controls are needed in a month.

(1) The first is to wait until >25 cases are enrolled in the month and then enroll extra controls as needed.

(2) The second strategy is to enroll extra controls when more than 7 cases are enrolled per week. Because this strategy matches on a smaller unit of time, the representativeness of the controls with respect to timing of circulating pathogens might be improved over the first option. The number of extra controls will be the number of excess cases beyond 7 cases in that week. The field supervisor should determine every week the number of extra controls to be enrolled. There will be a one week lag between the weekly number of cases enrolled and the equivalent number of controls enrolled. This could create a possible situation where more controls than cases are enrolled in a month if fewer cases are enrolled later in the month; however, this will not create a statistical problem.

(3) The third and perhaps logistically easiest strategy is to base monthly control enrollment rates on the number of cases seen in the previous year. Adjustments may have to be made with this strategy, though, as the number of cases as defined by PERCH criteria may differ, and rates may differ year to year. Weekly case and control enrollment rates should be monitored. Adjustments should be considered if cumulative bi-weekly imbalances are excessive (i.e., +/- 5).

1.1.6.2 The field supervisor will inform field workers how many extra controls will need to be enrolled. Extra controls will be moved *sequentially* from the backup control list to the active control list. For example, control #26 on the backup control list must be moved to the active list before #27. Not selecting controls from the backup list in sequential order has the potential of introducing bias. However, if 2 or more controls are moved from the back-up list to the active list, these can be approached for enrollment in any order. Similarly, once moved to the active list, any control still on the active list can be approached for enrollment without regard for order number. For example, if 15 cases were enrolled by week 2 (i.e., 3 in excess of the 12 expected), then 3 controls (#s 26, 27, & 28) can be moved to the active list and can be enrolled before control #6 if that control has not been enrolled yet.

1.2. Selection of controls in sites without DSS or birth registry of catchment area (Zambia, Mali, Thailand).

1.2.1. First stage of sampling

1.2.1.1. Segments will be defined as villages, quarters, or other established geographic units.

1.2.1.2. A list of randomly selected segments from the catchment area will be selected at the beginning of every month. These segments will be selected by simple random sampling with a probability proportional to size (see Immunization Coverage Cluster Survey, pages 63-65). If all segments are

approximately the same size, then it is not necessary to select them with a probability proportional to size.

1.2.1.3. The number of segments selected should be based on the number of controls anticipated for that month. Each month should have a minimum of 25 segments selected (to enroll the minimum number of 25 controls per month) – these will make up the active list. Extra segments should be generated on a back-up list in the event more than 25 controls are needed. If only 25 controls are enrolled in a month, only the first 25 segments on the active list will be used.

1.2.1.4. The same segment might be selected more than once.

1.2.1.5. Segments on the active list (i.e., within the first 25) can be sampled in any order. For example, segment 5 can be sampled prior to segments 1-4.

1.2.1.6. If more than 25 cases are enrolled in that month, then the backup list of segments should be used in sequential order (e.g. 26th, 27th, etc) to match the number of excess cases enrolled that month. See 1.1.6 above for determining if more than 25 segments are required.

1.2.2. Second stage of sampling (Zambia, Mali)

1.2.2.1. The selected segments will be sub-divided into smaller units, such as census enumeration areas. The sub-units should be approximately the same size and have approximately 100 households.

1.2.2.2. Assuming sub-segments are equal in size, one sub-segment within the selected segment will be selected at random. If not equal in size, subsegments should be selected with a probability proportional to size (see Immunization Coverage Cluster Survey, pages 63-5)

1.2.2.3. The age distribution of control children in the four age groups -- 0-5 months, 6-11 months, 12-23 months, and 24-59 months – should be the same as the distribution of cases determined in step 1.1.1. This can be done by randomly assigning an age category in the desired distribution to the selected sub-segments. The field team will select a child of the pre-determined age group in each sub-segment. Alternatively, children can be enrolled in any age group in the initial sub-segments. The field team must keep track of the number of children enrolled in each age group so by the end of the month's enrollment they will have enrolled the required number in each age group.

1.2.2.4. In each selected sub-segment a random starting point will be selected (by GIS or the random walk). (see Immunization Coverage Cluster Survey, pages 21-23). In brief, the random walk method dictates finding the center point of the sub-segment and choosing a direction at random, such as spinning a bottle. Then walking in a straight line in the direction that bottle points to the perimeter of the sub-segment, enumerating all household that fall along the path of the walk. Care should be taken not to deviate from the chosen direction by walking along established paths or roads. From the households enumerated during the walk, one household will be selected at random. This household will serve as the starting point.

1.2.2.5. An eligible child will be sought in the house closest to the starting point. If an eligible child is not found, the next house will be selected in a systematic manner, according to the Immunization

Coverage Cluster Survey, (e.g. the next house on the left). An eligible child will be sought in that house. This should be continued until an eligible child is identified. When an eligible child is found, the availability assessment and eligibility assessment should be done as described above (section 2.2-2.3).

1.2.3. Second stage of sampling (Thailand)

1.2.3.1. Using the registry of births in the selected village, one child will be selected at random. This child will be approached for enrollment. If he/she is not enrolled, a second child will be randomly selected for enrollment. This process will continue until a suitable control child is enrolled.

3. Identifying eligible controls. (Field team)

3.1. Go to the home of a child on the Active Control List.

3.2. Assess availability of the primary caregiver and child. If not at home but still in the area, then at least one revisit should be made when child is likely to be home. This information can be obtained from family members at home or neighbors. If information is obtained that the child will not be home for several days, the child can be marked as “not at home” on the Control Screening and Enrollment Log.

3.3 Eligibility assessment. Confirm that child meets inclusion criteria and does not meet exclusion criteria for controls.

3.3.1. Inclusion criteria

- Aged 28 days-59 months (If a randomly selected child is < 28 days old at the start of the month, then that child should be visited later in month after they reach 28 days old. On the other end of the age spectrum, if a child is 59 months old at the time of randomization, they should be visited before they reach 60 months of age and are no longer eligible.)
- Lives in the defined study catchment area (may be defined as a district, village or distance zone from the hospital)
- Accompanied by written informed parental/guardian consent

3.3.2. Exclusion Criteria

- Discharged from hospital within the last 14 days
- Severe/very severe pneumonia
- <30 days from admission date of previous enrollment as a case

3.3.3. Document eligibility assessment on CRF Form 1A: Community Control Screening and Enrollment Form.

3.3.4. Document eligibility status on the Control Screening and Enrollment Logs.

3.3.5. If eligible, proceed to 3.4.

3.4 Consent. If child meets eligibility criteria, get informed consent from parent or designated caretaker.

- For sites that will enroll in the field, consent will occur in the field.

- For sites that will enroll in the hospital, refer the child to the hospital by scheduling a visit date and time. Consent can be obtained either in the field or at the hospital prior to enrollment.

3.5. After consent has been obtained, proceed to data collection forms for controls. (See section 6).

6. Data collection from controls

6.1. Enrollment in clinic.

6.1.1. Re-evaluate eligibility criteria for children presenting.

6.1.1.1. If control child meets definition of severe/very severe pneumonia they should be not enrolled as a control. If they are eligible to be a case, they should be referred for case enrollment by the team doing enrollment. Note that children with non-severe pneumonia can be enrolled as controls.

6.1.2. Get informed consent from guardian.

6.1.3. Complete CRFs: Form 1A: Community Control Screening and Enrolment Form
 Form 2: demographics
 Form 3: clinical history
 Form 4A: clinical assessment
 Form XX-XX: Control specimen collection forms

6.1.4. Collect required specimens.

6.2. Enrollment in home

6.2.1. If control child has signs/symptoms of severe or very severe pneumonia, they should be referred to hospital, preferably to the PERCH hospital for clinical evaluation and possible enrollment into PERCH. Do not enroll children with suspected PERCH definition of severe/very severe pneumonia. Children with non-severe pneumonia can be enrolled but these children should also be referred to health facilities for assessment and care after enrollment.

6.2.2. Get informed consent from guardian.

6.2.3. Complete CRFs: Form 1A: Community Control Screening and Enrolment Form
 Form 2: demographics
 Form 3: clinical history
 Form 4A: clinical assessment
 Form XX-XX: Control specimen collection forms

6.2.4. Collect required specimens.

7.0 Compensation.

THE SITES COMPENSATION POLICY FOR CONTROLS GOING TO CLINIC SHOULD BE OUTLINED HERE.

8. Specimen transport. See specimen transport SOP.

9. Control enrollment log. Tick off the controls that were enrolled from the control enrollment log after you are done with control enrollment.

10. HIV-positive controls (SA and Zambia)

10.1. For each HIV-infected case enrolled, an HIV-infected control will be enrolled. This is separate from enrollment of the 25 monthly controls described above. The HIV-infected control should be in the same age group (0-5 months, 6-11 months, 12-23 months, and 24-59 months) as the case. The control will also be matched to the case on the level of routine HIV care received. Whether the HIV-infected case is a regular attendee of an HIV-care clinic should be determined. This is defined as having made ≥ 2 visits in the last 3 months. By definition, this means the child's HIV-positive status was known prior to the PERCH admission. The second type of child with HIV infection will be either newly diagnosed during the hospital admission or HIV-diagnosed but not attending the HIV care clinic.

10.2. HIV-infected controls will be enrolled at the HIV care clinics located in the catchment area. While not all HIV care clinics in the catchment area need be included, more than one HIV care clinic should be used, preferably with a representative geographic distribution of the catchment area. The distribution of controls enrolled in each HIV care clinic should be similar geographically to the cases, as much as possible.

10.3. Two types of HIV-infected children will be enrolled in the HIV care clinic. The first will be children newly diagnosed with HIV infection. These will be matched to those children admitted to the PERCH study who were newly diagnosed with HIV or HIV-diagnosed but not attending the HIV care clinic. The second type of HIV-infected control will be children receiving regular care at the HIV care clinic (defined as ≥ 2 visits in the past 3 months.) These will be matched to those children admitted to the PERCH study who are receiving regular care at the HIV care clinic.

10.4. CD4 counts. CD4 counts obtained within the past 3 months in the HIV care clinic can be used. If not available in this time period, then a new CD4 count should be taken on the control at the time of enrollment.



► Standard Operating Procedure ◀

Section: Clin Epi

Version: FINAL

Initials: KOB

Title: Chest X-Ray

Revision Date: January 4, 2011

1.0 Purpose/Introduction:

The purpose of this Standard Operating Procedure (SOP) is to outline the processes and performance of CXR collection, scanning and film reading in the PERCH study.

2.0 Scope/Responsibility:

2.1 **CXR Performance:** This SOP applies to the X-ray department and clinical facilities at [*state the facilities where CXRs are done*] where CXRs may be conducted.

2.1.1 **Radiographers:** Radiographers are responsible for ensuring the regular maintenance, adequate functioning and safe performance of radiological equipment. Radiographers are responsible for the safety of patients, parents/guardians, and staff during radiologic procedures including the use of lead shields where appropriate, providing gonadal and thyroid shields where appropriate, ensuring correct radiological doses for the procedure, and ensuring constant dosimeter use by radiology staff and maintenance of the logs. Radiographers are also responsible for performing the CXR on the study children.

2.1.2 **Study clinicians:** Study clinicians are responsible for identifying subjects who meet criteria for obtaining a CXR. Study clinicians are also responsible for requesting that a CXR be performed on relevant study subjects.

2.1.3 **Porters:** are responsible for transporting children to the radiology department

2.2 **CXR Digital Image Collection:**

2.2.1 Scanning of hard films: This SOP applies to the [*state the study staff who will do the scanning*] who are responsible for scanning CXR hard films (for facilities without digital radiography).

2.2.2 Collecting digital CXR images: This SOP applies to the [*state the study staff who are responsible for collecting the digital images*] who are responsible for downloading and storing in study files the digital CXR images (for facilities with digital radiography).

2.3 **CXR Reading:** This SOP applies to the study radiologist and study physicians who will be reading the films according to the WHO reading procedures for the study purpose.

3.0 Abbreviations/Definitions:

- CXR: Chest X-Ray
- TachKV: kilovolt
- mAs: milli ampere

4.0 Methodology:

4.1 Indication for CXR: Study clinicians will order a CXR on all subjects who are to be enrolled in the PERCH study as cases. The study clinician will complete a CXR request form (*need specifics here on the study forms to complete*) and alert the radiology department that a CXR is needed. Depending on the acuity of the child's illness the child will be transported to the radiology department or a portable film will be conducted. All films will be done at the time of admission of the child to hospital or as soon as possible thereafter but within 72 hours.

4.2 Equipment

- 4.2.1 Lead shields: To shield gonads of children and to shield gonads, thyroid of parent/caretaker of child.
- 4.2.2 Radiology equipment:
- 4.2.2.1 Digital radiography: TO BE SPECIFIED FOR EACH SITE
- 4.2.2.2 Analog radiography: TO BE SPECIFIED FOR EACH SITE
- 4.3 Performance of CXR:
- 4.3.1 Preparation of study subject
1. Study subject is brought to the radiology department if sufficiently stable. If not sufficiently stable a portable CXR is obtained.
 2. Radiographers check subject identification against CXR request to assure the right child is having a CXR obtained
 3. Patient and accompanying person are provided with lead shields and procedure is explained
 4. Appropriate exposure is done and radiographer puts cassettes in place
 5. Patient is positioned properly and procedure is carried out at correct radiologic dose
 6. Radiographer explains end of the procedure and patient with parent/guardian returns to clinical treatment area
 7. Radiographer processes the cassettes
 8. Images are reviewed by XXXX for adequacy of film
 9. Treating clinician is notified that film is ready
 10. Study clinician obtains image of film
- 4.3.2 Chest anterior-posterior supine
- Infants weighing up to 10 kg and older children who are unable to have an erect film collected will have a supine film taken.
- Cassette speed: cassette with screen film combination, nominal speed 200 on cassette holder
 - Cassette size: 18 x 24 cm (8 x 10 inches)
 - Use Right or Left marker
 - Exposure volume: 63 KV; 2.5 mAs
- 4.3.2.1 Technique:
- Center the cassette on top of the cassette holder. Collimate to the format.
1. Lie the infant in his/her back on the cassette with legs and head supported.
 2. Use a protective lead strip over the infant's pelvic area.
 3. Those accompanying and holding the infant (preferably the parents) must wear lead aprons and wherever possible, lead gloves.
 4. Center between the nipples. Collimate further, if possible.
 5. Expose when infant is not moving, preferably on inspiration.
- 4.3.3 Chest posterior-anterior erect
- Infants and small children over 10 kg, held by the upper arms.
- Cassette speed: cassette with screen film combination, nominal speed 200 in the cassette holder

- Cassette size: 24 x 30 cm (10 x 12 inches)
- Use Right or Left mark
- Exposure volume: 77 KV; 3.5 mAs range

4.3.3.1 Technique

Put the cassette in the cassette holder. Collimate to the format.

1. Position the child: The child is held hanging by the upper arms and if possible support the feet with a stool or the floor or someone holding the thighs. Rest the child's back against the front of the cassette holder
2. Use a protective lead strip over the infant's pelvic area.
3. Those accompanying and holding the infant (preferably the parents) must wear lead aprons and wherever possible, lead gloves.
4. Center between the nipples. Collimate further, if possible.
5. Expose when infant is not moving, preferably on inspiration.

4.4 Scanning of CXR hard films:

4.4.1 Equipment: (a) Computer with Windows 2000, or Windows XP and dicomPACS software (b) Scanner: Epson Expression 10000 XL

4.4.2 Procedure

1. Bring the hard film to the scanner set up
2. Switch on the computer; type in the username in small letters: **scanner** and password: **xxxxxxx**
3. Click on the program icon named: **dicomPacs**
4. Press "S": For scan
5. Lay x-ray on the flatbed scanner. Close lid of scanner.
6. Click on Preview
7. Select the part of the image wanted using the mouse. Include the lung fields, make sure the clavicles are visible.
8. Press "Scan"
9. After scan is complete, click on "Close"
10. Press "A": For Archiving the image
11. Type in the details of the patient: **Unique PERCH Participant ID number and Date** as well as the Description (PA or lateral or decubitus)
12. Click on "Archive"

13. Click on **F9** – To review the archiving of the x-ray

14. Close the program

15. Remove CXR from the scanner and return film to radiology department

4.5 Reading of CXR

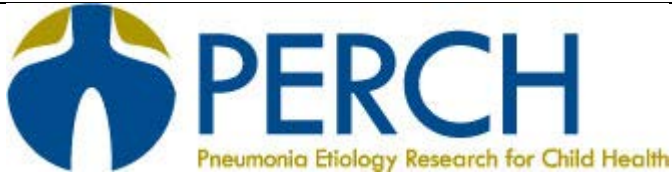
1. The CXR will be assessed by the radiographer or the treating clinician as sufficient for clinical use.
If insufficient for clinical use the film will be repeated.
2. For study purposes, the following steps will be followed.
 - a. identify the digital image of the CXR to be read including the unique study identification number.
 - b. The CXR will be read by 2 readers (clinicians/radiologists), adequately trained to read the CXR as per the “Standardization of interpretation of chest radiographs for the diagnosis of pneumonia in children” by the WHO (Appendix X)
 - c. Assess quality of the CXR (see Appendix 5.1)
 - d. Classification of findings (see Appendix 5.1):
 - 1 = primary end-point consolidation or pleural effusion
 - 2 = Other consolidation/infiltrate
 - 3 = Normal film
 - e. Record the CXR study readings of film quality and findings on XXXXX

4.5.1 Quality Assurance Processes

1. All films will be read by a study clinician and study radiologist trained in the WHO reading framework
2. Readings will be done quarterly
3. Concordance is defined as agreement on the presence or absence of the primary endpoint.
4. A reference panel of two radiologist trained in the WHO reading framework will be established. They will review all CXRs that are not concordant and of the concordant they will also review 10% of the films classified as ‘1’ and 10% of the films classified as ‘2’.
5. For discordant films, the reading of the Reference Panel will be taken as the final reading.
6. For the concordant films that are read by the Reference Panel, the final reading is that of the site readers but the results are fed back to the site readers.

4.6 Training

The Site PI and the PERCH Core PI are responsible for the availability of training. Training will be documented by signing training logs. All clinical staff involved in the process will have been trained in the SOP and their respective duties.



► Standard Operating Procedure ◀

Section: Clinical/Epidemiology

Version: FINAL

Initials: NF

Title: CXR Online Interpretation

Revision Date: 10 Apr 2013

1.0 Purpose/Introduction:

The purpose of this Standard Operating Procedure (SOP) is to outline processes for the interpretation of Chest X-Rays (CXRs) by trained readers and arbitrators.

2.0 Scope/Responsibility:

2.1 This SOP applies to PERCH study CXR readers and arbitrators

3.0 Abbreviations/Definitions:

- CXR: Chest X-Ray
- Reader: A physician or radiologist certified in the WHO methodology for the interpretation of pediatric CXRs and providing such interpretations for the PERCH project
- Arbitrator: A technical expert member of the PERCH CXR arbitration and training panel
- Reviewer: Inclusive of both readers and arbitrators interpreting images
- eCRF: Electronic Case Report Form
- EMMES: The data management company delivering the online platform for CXR viewing and interpretation
- AdvantageEDC: The electronic data capturing system used for PERCH and administered by EMMES

4.0 Prerequisites/Supplies Needed:

4.1 Initial training on the WHO methodology for the interpretation of pediatric CXRs

4.1.1 All readers must have undertaken an initial training in this methodology, as adapted for PERCH purposes, and successfully interpreted a set of images for standardization

4.2 Ongoing education and certification

4.2.1 CXR readers are required to complete periodic online refresher certification quizzes. This will consist of 20-30 images with feedback on results and reference diagnoses provided.

4.2.2 Every six months, and additionally if required, formal online training modules will be delivered to help refresh and clarify the WHO methodology

4.3 Computer Equipment and Environment

4.3.1 Readers and arbitrators need access to a computer (preferably with a high quality LCD screen) and stable internet access to complete online interpretations

4.3.2 CXR readings should ideally be done in the same environment throughout the study, with low levels of ambient light. Reviewers are responsible for ensuring the appropriateness and consistency of their environment when interpreting CXR images

4.3.3 Setup of monitors: All reviewers have a copy of the **SMPTE Test Pattern**, which is also available on the AdvantageEDC CXR Evaluation webpage. This should be opened (full-screen) before beginning interpretations to ensure the calibration and optimization of the viewing screen. Evaluate the SMPTE pattern with the following criteria:

- a. Grayscale squares should be easily differentiated at each step, 0% through 100%.
- b. High and low contrast resolution patterns should be of high integrity in the center and all four corners.
- c. 95% - 100% and 0% - 5% squares should have visible darker/lighter patches inside them

- d. Grid lines should be straight with no distortion.
- 4.3.4 Browser configuration: Step-by-step documentation for setting up IE, Safari, and Firefox browsers is available at:
https://web.emmes.com/study/perch/protocol/xray/Browser_Configuration_post-IDES19.pdf

5.0 Use of AdvantageEDC for accessing CXR images

5.1.1 Accessing AdvantageEDC

- a. The AdvantageEDC platform can be accessed via the Data Entry System link from the EMMES study website (separate credentials to access the website and the data system will be provided to all reviewers):
<https://web.emmes.com/study/perch/protocol/xray/xray.htm>
- b. All reviewers will complete and submit an eCRF capturing the evaluations for each image assigned to them in the database.
- c. Full details on accessing and navigating the CXR interpretation system in AdvantageEDC are provided in the “CXR Evaluation Process User’s Guide” available for download on the CXR Evaluation Page of AdvantageEDC

6.0 Reporting of Protected Health Information (PHI) data or incorrect file type

- 6.1 All CXR images presented in AdvantageEDC have been through several checks at the site, core team, and EMMES levels to ensure the absence of any PHI data. If, however, any such data is noticed readers and arbitrators should immediately inform the PERCH core team and EMMES by emailing nfancour@jhsph.edu and perch@emmes.com with the file details.
- 6.2 All CXR images should be either AP or PA orientation. Any lateral or decubitus films should be noted and the PERCH team informed by emailing nfancour@jhsph.edu. These images will not be included in the AdvantageEDC review process.
- 6.3 Technical problems with the viewing of images, or navigation through the AdvantageEDC process, should be directed to perch@emmes.com in the first instance.

7.0 WHO Methodology and Conclusions

- 7.1 For the purposes of PERCH and its focus on pneumonia etiology (as opposed to vaccine impact) the interpretation conclusions have altered slightly from the original WHO format. **The definitions and questions remain largely unchanged. Readers are encouraged to refer to their materials and notes from the training meeting on the WHO methodology.**
- 7.2 Interpretation questions: Each CXR will be reviewed for four questions:
 - a. Primary Consolidation (left/right/bilateral/none/uninterpretable)
 - b. Other infiltrate (left/right/bilateral/none/uninterpretable)
 - c. Pleural effusion (left/right/bilateral/none)
 - d. Orientation concerns (yes/no)

** There is no ‘uninterpretable’ category for pleural effusion. Unless a reader is certain of the presence of an effusion the answer should be ‘no’ (including where the costophrenic angle is not present on the film due to cropping or coning of the image). This avoids any complications where pathology is identified but readers are uncertain of whether pleural effusion is absent or uninterpretable. For instance, where primary consolidation may be present but an effusion ‘uninterpretable’.*
- 7.3 The first three of these questions help to inform a final conclusion on the interpretation of the CXR. This can take one of five categories:
 - a. Primary end point pneumonia only
 - b. Other infiltrate only
 - c. Both primary end point pneumonia and other infiltrate

- d. Normal
- e. Uninterpretable

** For clarification, a CXR may be uninterpretable for one question (eg other infiltrate) but have pathology identified in another (eg primary consolidation). In such a case the pathology is reported as the overall conclusion. Only uninterpretable films with no identified pathology, or uninterpretable for both primary consolidation and other infiltrate, will reach a primary conclusion of 'uninterpretable'.*



► **Standard Operating Procedure** ◀

Section: Clin Epi

Version: FINAL

Initials: _____

Title: Gastric Aspiration

Revision Date: January 15, 2010

1. Definitions

1.1. N/A

2. Purpose / Background

2.1. Gastric aspiration is a technique used to collect gastric contents to try to confirm diagnosis of TB by microscopy and mycobacterial culture. Because of the distress caused to the child, and the generally low yield of smear-positivity on microscopy, this procedure should only be used where culture is available as well as microscopy.

3. Scope / Applicability

3.1 This SOP applies to clinicians, nurses and laboratory staff involved in carrying out the procedure of gastric aspiration and the handling of the aspirate sample.

4. Prerequisites / Supplies Needed

4.1

- Gloves
- Nasogastric tube (usually 10 French or larger)
- 5, 10, 20 or 30 cm³ syringe, with appropriate connector for the nasogastric tube
- Litmus paper
- Specimen container
- pen (to label specimens)
- Laboratory requisition forms
- sterile water or normal saline (0.9% NaCl)
- Sodium bicarbonate solution (8%)
- Alcohol/chlorhexidine

5. Roles / Responsibilities

5.1 Clinicians and nurses are responsible for performing this procedure

6. Indications, Contraindications and Safety:

6.1 **INDICATIONS:** Gastric aspirates are used for collection of samples for microscopy and mycobacterial cultures in young children when sputa cannot be spontaneously expectorated nor induced using hypertonic saline.

6.2 CONTRAINDICATIONS:

- 6.2.1 Inadequate fasting (<4hrs ;< 3hrs in infants)
- 6.2.2 Platelet count <50 × 10⁹/l
- 6.2.3 History of severe nosebleeds or any other bleeding tendencies.

6.3 **SAFETY:** Gastric aspiration is generally not an aerosol-generating procedure. As young children are also at low risk of transmitting infection, gastric aspiration can be considered a low risk procedure for TB transmission and can safely be performed at the child's bedside or in a routine procedure room.

7. Procedural Steps:

7.1 The procedure should be carried out as an inpatient first thing in the morning when the child wakes up, at the child's bedside or in a procedure room on the ward. The child should have fasted for at least 4 hours (infants for 3 hours) before the procedure.

- 7.1.1 Find an assistant to help.
- 7.1.2 Prepare all equipment before starting the procedure.
- 7.1.3 Position the child on his or her back or side. The assistant should help to hold the child.
- 7.1.4 Measure the distance between the nose and stomach, to estimate distance that will be required to insert the tube into the stomach.
- 7.1.5 Attach a syringe to the nasogastric tube.
- 7.1.6 Gently insert the nasogastric tube through the nose and advance it into the stomach.
- 7.1.7 Withdraw (aspirate) gastric contents (2–5 ml) using the syringe attached to the nasogastric tube.
- 7.1.8 To check that the position of the tube is correct, test the gastric contents with litmus paper: blue litmus turns red (in response to the acidic stomach contents). (This can also be checked by pushing some air (e.g. 3–5 ml) from the syringe into the stomach and listening with a stethoscope over the stomach.)
- 7.1.9 If no fluid is aspirated, insert 5–10 ml sterile water or normal saline and attempt to aspirate again. If still unsuccessful, attempt this again (even if the nasogastric tube is in an incorrect position and water or normal saline is inserted into the airways, the risk of adverse events is still very small). Do not repeat more than three times.
- 7.1.10 Withdraw the gastric contents (ideally at least 5–10 ml).
- 7.1.11 Transfer gastric fluid from the syringe into a sterile container (sputum collection cup).
- 7.1.12 Add an equal volume of sodium bicarbonate solution to the specimen (in order to neutralize the acidic gastric contents and so prevent destruction of tubercle bacilli).

7.2 After the procedure:

- 7.2.1 Wipe the specimen container with alcohol/chlorhexidine to prevent cross-infection and label the container.
- 7.2.2 Fill out the laboratory requisition forms.
- 7.2.3 Transport the specimen (in a cool box) to the laboratory for processing as soon as possible (Within 4 hours).

7.2.4 If it is likely to take more than 4 hours for the specimens to be transported, place them in the refrigerator (4–8 °C) and store until transported.

7.2.5 Give the child his or her usual food.

7.3 Specimen Transport and Storage:

Specimen	Transport/storage conditions*	Until
Gastric Aspirate	≤24 h, 4°C (≤15 min, room temperature)	TB culture

8. Record Management

9. Quality Assurance / Quality Control

10. References

9.1. WHO, Guidance for national tuberculosis programmes on the management of tuberculosis in children. WHO, Geneva 2006.

	► Standard Operating Procedure ◀
Section: Clin Epi	Version: FINAL Initials: MG/LLH/KOB
Title: Induced Sputum	Revision Date: 29 Oct 2013

1. Definitions

1.1. Abbreviations

- IS – induced sputum
- MTB – *Mycobacterium tuberculosis*
- MDI – metered dose inhaler
- SOP – standard operating procedure

1.2. Hypertonic saline: 5% saline.

1.3. First induced sputum – Will be collected from all cases except those with contraindications.

1.4. Second induced sputum – A second IS will be performed ≥ 24 hours after the first IS in children with suspected TB. Criteria for Suspected TB include any of the following:

- pneumonia which fails to respond to 48 hours of first line antibiotics;
- living in the same household as, or in frequent contact with, a suspected or confirmed case of pulmonary TB;
- persistent, unremitting cough for >2 weeks;
- unexplained fever for >2 weeks;
- unexplained progressive weight loss or failure to thrive for >4 weeks;
- doctor’s clinical suspicion of TB.

2. Purpose / Background

2.1. Sputum induction is collection of an adequate sample of secretions from the lower respiratory tract in children who do not produce sputum spontaneously.

2.2. Undertaken in a child with clinical evidence of pneumonia.

2.3. The aim is to induce deep coughing by inhalation of an aerosol of hypertonic saline.

2.4. Used for tuberculosis diagnostics, microscopy, bacterial culture and susceptibility testing, and multiplex PCR, including PCP testing.

2.5. The SOP is necessary to ensure that specimen collection is carried out in a systematic and accurate way while ensuring the safety and welfare of the participants.

3. Scope / Applicability

3.1. The SOP will be utilized by the clinic research staff including medical doctors, nurses and physiotherapists

3.2. Induced sputum will be collected from all cases except those with contraindications (see 3.3). A second induced sputum will be performed on those cases in whom TB is suspected (see 1.3).

3.3. Contraindications:

- Severe hypoxia (<92% on supplemental oxygen)
- Inability to protect airways
- Severe bronchospasm at admission
- Seizure within the past 24 hours
- Deemed inappropriate by the clinician for another reason (e.g., mid-face trauma, inhalational injury, pulmonary effusion, congestive heart failure, congenital heart disease, etc).

If the above symptoms/conditions resolve during hospital course, IS collection may be reconsidered at that point.

Note: Caution should be exercised when performing induced sputum procedures on children with an AVPU score of V, P, or U. Children with a score of <A may be more likely to be very ill and to face clinical deterioration regardless of whether an induced sputum sample is collected. If induced sputum procedures are performed on a child with a score of <A, care should be taken when introducing PO feeds as these children may be more likely to aspirate upon feeding.

4. Prerequisites / Supplies Needed

4.1. Prerequisites

- The procedure may only be carried out by trained, designated study staff after the procedure has been explained to the parent/guardian and child and permission has been granted. The procedure

will be performed by a nurse, clinical officer, or medical officer. Field workers may assist with this procedure.

- The first induced sputum should be collected within 48 hours of admission (preferably within 24 hours). The second induced sputum should be done the following day, or if this is not possible, at least 4 hours after the initial sample has been collected.
- The appropriate infection control precautions will be taken to prevent infection with MTB via droplet inhalation:
 - The study staff member will wear a surgical mask and gloves, which will be changed in between patients. If a FFP2 or N95 mask is available, the staff may wear a surgical mask over the FFP2 or N95 mask. If this technique is used, the surgical mask being worn over top of the FFP2 or N95 should be changed between patients, but the FFP2 or N95 mask may be worn by the staff member without being changed between patients.
 - The procedure will be done in a well-ventilated area.
- The child should have been fasting for 3 hours prior to the procedure.

4.2. Supplies needed

Salbutamol/albuterol metered dose inhaler	100 µg / puff
Spacer device with mask	e.g. aerochamber
Facemask with chamber connected via tubing to a nebuliser device, OR to oxygen mixer.	
Sterile hypertonic saline	5ml
Normal saline flush	5 ml
Suction apparatus device	automated or manual depending on availability
Closed loop mucous extractor	
Mask	preferably N95 or FFP2 for personnel performing the IS; surgical mask is an acceptable alternative
Disposable non-sterile gloves	
Case specimen collection form	
Resuscitation trolley with adrenaline	
Catheter	8 Fr for most children; 6 Fr for infants <3 months (recommended)
Respiratory rate timer	

5. Roles / Responsibilities

- 5.1. Clinical staff – nurse, doctor or physiotherapist will perform all aspects of the procedure.

6. Procedural Steps

- 6.1. Explain the procedure to the parent/guardian and ask for verbal consent.
- 6.2. Wash hands with anti-septic soap/solution and dry them using a disposal paper towel.
- 6.3. Put on a clean pair of disposable gloves.
- 6.4. Note the pre-procedure respiratory status (O₂ saturation by pulse oximetry, oxygen requirement, and respiratory rate). The pulse oximeter should be kept on the child continuously during the course of the procedure to monitor for significant desaturation (defined as oxygen saturation <92%). If the child's pulse ox goes below 92% or if otherwise clinically indicated, additional oxygen should be delivered to increase the pulse ox to 92% or above.
- 6.5. The procedure must be **stopped** in the following situations:
 - 6.5.1 Oxygen saturation drops to $\leq 88\%$ for at least 60 seconds. The 60 seconds is needed to verify that the reading is accurate and not a result of some artifact or momentary fluctuation in the oximeter.
 - The procedure will be stopped..
 - Increase the oxygen delivery and other appropriate clinical measures to re-establish oxygen saturation levels to $\geq 92\%$.
 - If after a period of stabilization/rest the child's respiratory status improves so they are back to their baseline status at the start of the procedure the IS procedure can be reinitiated
 - O₂ saturation must be stable and $\geq 92\%$ for five minutes or more
 - If the O₂ requirement remains greater than at the beginning of the procedure, the procedure may be restarted only after careful clinical evaluation about the magnitude of change in oxygen requirement, the clinical stability of the child and disease progression.
 - 6.5.2 Oxygen saturation falls to 89-91% for more than 60 seconds despite increase in supplemental oxygen.
 - If the child's oxygen saturation can be reestablished over 92% with supplemental oxygen within 60 seconds, the procedure can continue without stopping.
- 6.6 Children receiving supplemental oxygen via nasal cannula should be continued on the supplemental oxygen during the course of the procedure.

- 6.7 Clear any secretions from the anterior nares with a tissue or suction device before collecting the IS sample. If a suction device is used, dispose of it. Do not use the same suction device to collect the specimen.
- 6.8 Connect the specimen collection device to a foot or electric pump.
- 6.9 Bronchodilator administration: To facilitate bronchodilation and minimize bronchospasm from the nebulized hypertonic saline, a β -2 agonist (salbutamol or albuterol) will be given ~5 minutes prior to nebulization with hypertonic saline. This will be done by administration of two puffs, spaced 10 seconds apart, using a metered dose inhaler (MDI - 100 μ g / puff) via a spacer device such as an aerochamber or via nebulisation.
- 6.10 Following administration of the β -2 agonist the child will then be nebulised with 5 mls of sterile hypertonic saline [5% NaCl] solution using a facemask with an attached aerochamber. Nebulisation may occur with the use of a jet nebuliser, or using mixed oxygen flow at a rate of 5-8 l/min. Nebulisation should be continued until all the hypertonic solution has emptied from the chamber or alternately for at least 10 minutes.
- 6.11 Percussion of the chest wall will be performed in children <24 months of age during hypertonic saline nebulisation, and is optional in older children in the absence of hypertonic saline having induced the child to cough. Percussion of the posterior aspects of the upper and lower quadrants of the left and right chest walls can be undertaken using a cusped hand or rubber face-mask. Each quadrant of the posterior aspect of the chest should be tapped gently 5-10 times to help mobilize lower respiratory secretions and induce a cough in the child.
- 6.12 Once the child starts coughing, start the respiratory rate timer and insert the catheter through the nose into the nasopharynx. A catheter connected via a closed loop mucus extractor to a suction device is the preferred method of collection of the mucus. An alternate (although less satisfactory) method is to use a nasopharyngeal tube attached to a 10 ml syringe to which suction is applied when the child starts expectorating.
- 6.12.1 Once the catheter is inserted into the correct position, apply suction.
- 6.12.2 Do NOT repeatedly advance and withdraw the catheter within the nasopharynx.
- 6.12.3 Remove the catheter without applying any suction (to avoid aspirating anterior nasal contents) when either of the following has taken place:
- a. Secretions have half-filled the suction catheter (~0.5 ml)

OR, (whichever occurs first),

- b. A maximum of 30 seconds have elapsed (respiratory rate timer beeps once; **NOTE**: you should, however, aim to remove the catheter in <10 seconds, to avoid traumatizing the child).

- 6.13 Aspirate approximately 5 mls of sterile normal saline to flush the tube. (NB: do not use the hypertonic saline that was used for nebulisation)
- 6.14 Once the secretions have been collected the sample should be sent immediately to the laboratory for further aliquoting into sterile specimen containers.
- 6.15 Continuous pulse oximetry should be continued following the procedure for 30 minutes. Following this, the child's respiratory status will be followed at 2 hours and 4 hours after the procedure (or more frequently, if there is a clinical indication)
- 6.16 Specimens should be sent to the laboratory within 8 hours of collection with the appropriate requisition forms completed.

Precautions:

In case of increasing respiratory distress, including desaturation to <92% or audible wheezing, the induced sputum procedure should be terminated and the child placed immediately on supplemental oxygen therapy, if not already on it, either by nasal cannula or alternatively by facemask. If the child is already on oxygen, the amount of oxygen being delivered should be increased to increase the oxygen saturation at least to 92%. In addition, a β -2 agonist (salbutamol or albuterol) should be administered by aerochamber or via nebulization. A doctor on call should be notified immediately to evaluate the child.

Clinical staff will periodically attempt to wean the amount of oxygen being delivered (if clinically appropriate) to assess whether or not the increased oxygen requirement is persistent.

Safety monitoring:

Record the child's oxygen requirement, oxygen saturation, respiratory rate and conscious level immediately prior to the procedure, immediately following the procedure and at 30 minutes , 2hrs and 4 hrs after the procedure on CRF 07 (Case Specimen Collection Induced Sputum).

If any of the following are observed **within four hours** following the induced sputum procedure - notify the local safety monitor and complete CRF 16 (SAE).

- Drop in oxygen saturation to below 92% resulting in a new or increased supply of supplemental oxygen for 10 minutes or more
- New onset of unconsciousness or prostration
- New requirement for bronchodilator
- Increased frequency of bronchodilator treatment
- Death

After the procedure:

- Disposable equipment is discarded into red 'biohazard' plastic bags for incineration at the end of the procedure.
- Equipment for re-use (nebulizer, spacer device, mask) is washed with in a dilute bleach solution and air dried for further use. Re-usable equipment must be cleaned between each patient.
- Study personnel should wear a clean mask for each patient. If using N95 or FFP2 masks, a surgical mask may be placed over the N95/FFP2 during the procedure and discarded after the procedure, allowing for the N95/FFP2 to be reused for multiple patients. The N95/FFP2 mask should be discarded at the end of a session.

Specimen Transport and Storage:

Specimen	Transport/storage conditions*	Until
Induced Sputum	≤24 h, 4°C	Inoculation onto culture media and other primary laboratory processing

7. Record Management

7.1. A case specimen collection form must be complete recording date of collection, time of collection and reason for IS not being performed if applicable.

8. Quality Assurance / Quality Control

- 8.1. All study fieldworkers, nurses and clinicians will be trained in this SOP. All nurses and clinicians that will collect specimens will also undergo practical training for IS collection. Study personnel will not be approved to collect IS until their competency has been assessed by a supervising clinician and signed off in the training log.
- 8.2. Refresher training will be conducted every 6 months at which time study staff will be required to demonstrate proficiency at IS collection.
- 8.3. The quality of the specimen will be assessed using the “Bartlett’s Score”. Specimens with suboptimal Bartlett’s Score will still be processed by the lab for all specified testing, but the Bartlett Score and consequent microbiology results will be considered in the analysis. Suboptimal Bartlett Scores will also be reported to the clinical team doing the procedure as a performance quality assurance indicator.

9. References

1. Lahti E, Peltola V, Waris M *et al*. Induced sputum in the diagnosis of childhood community-acquired pneumonia. *Thorax* 2009; 64(3):252-7.
2. Zar HJ, Tannenbaum E, Apolles P, Roux P, Hanslo D, Hussey G. Sputum induction for the diagnosis of pulmonary tuberculosis in infants and young children in an urban setting in South Africa. *Arch Dis Child* 2000; 82(4):305-8.

9.1 Supplementary Documents: Case Specimen collection form – Induced sputum and gastric aspirate.

	
Section: Clin Epi	Version: FINAL Initials: R Ideh/ B. Ebruke
Percutaneous Transthoracic Lung Aspiration	Revision Date: August 28, 2013

1. Definitions

SOP – standard operating procedure.

CXR – chest radiograph

Normal saline – 0.9% NaCl solution

2. Purpose / Background

The purpose of percutaneous transthoracic aspiration is to obtain a good quality sample for aetiological analysis directly from the site of infection. It is a sensitive and proven diagnostic method that aids the management of pneumonia.

This SOP is intended to ensure that the procedure is carried out to a set and reproducible standard providing for good quality samples and safety of patients.

3. Scope / Applicability

This SOP applies to clinicians, nurses and laboratory staff involved in carrying out the procedure of lung aspiration and the handling of the aspirate sample.

4. Prerequisites / Supplies Needed

- CXR
- Signed Informed consent
- Standard sterile dressing pack with galipots, kidney dish cotton wool and gauze
- Water source (running water)
- Sterile gloves
- 70% Alcohol
- Sterile 5ml syringe
- 21g hypodermic needles
- Sterile normal saline
- Sterile universal containers for aspirates
- Specimen label stickers
- Appropriate laboratory request forms
- Observation log sheets / charts
- Pulse oximetry
- Supplemental oxygen source and delivery equipment
- Equipment for chest intubation
- Sharps box

5. Roles / Responsibilities

Doctor/Clinician is responsible for ensuring eligibility and suitability of subject for lung aspiration. He/she will carry out the procedure and deliver the aspirate into the appropriate specimen containers.

Study nurse assists the clinician in carrying out the procedure and is responsible for the monitoring and documentation of observations pre and post aspiration. He/she ensures the relevant materials are available and the procedure room set up.

Field worker/clinical assistant transports the sample to the laboratory. Ensures the sample transfer logs are completed and signed.

Laboratory scientist receives the aspirate sample, completes the relevant transfer documents and carries out the necessary laboratory processing of the aspirate sample.

6. Contraindications

1. Presence of pneumatoceles on CXR
2. Post measles pneumonia.
3. If patient is clinically unstable as determined by a clinician, the procedure should be deferred until stabilization.
4. CPR performed within the last 24 hours.

7. Procedural Steps

- Check for accessible area of dense peripheral consolidation on CXR.
- Ensure there are no contraindications for lung aspirate: 1. the presence of pneumatoceles on CXR, 2. post measles pneumonia, 3. Deemed clinically unstable as determined by a clinician, 4. CPR performed within the last 24 hours.
- Stabilise the child by holding safely and firmly in the sitting or supine position.
- Confirm the location of consolidation seen on CXR by identifying the area of maximal dullness to percussion and/or maximal crepitations on auscultation.
- Wash your hands and wear sterile gloves.
- Clean the patient's skin with 70% alcohol using circular motions from the center to perimeter without returning to the previously cleaned site. Repeat this procedure at least once (more if necessary).
- **Allow this solution to AIR DRY.** Antisepsis will be achieved only if the solution is allowed to dry.
- Attach standard 21-gauge needle to a 5 ml syringe and aspirate 1ml sterile 0.9% Saline (normal saline).
- Insert needle **over the top** of the rib into the suspected area of consolidation at the point of maximal dullness to percussion and aspirate immediately, maintaining maximal suction pressure on the 5ml syringe while the needle is being withdrawn over about 2 seconds. (Inserting over the top of the rib avoids damaging vessels and nerves running underneath the rib).
- For upper lobe consolidation, use an anterior approach and for lower lobe lesions, a posterior approach is preferred.
- Flush out the syringe and attached hypodermic needle with the sterile normal saline into a universal bottle.
- Write the following on the specimen label in legible writing
 - The patient's name

- Study number
 - Date and time of collection
 - Collector's identification
- Transport specimen directly to the laboratory for processing.
- Observe the patient continuously for 15 minutes after the procedure looking for any sign of deterioration (significant changes in oxygen saturation, respiratory rate, respiratory distress, overall condition), then review every 30 minutes for 2 hours looking for any change before returning to standard observation interval. If there is any sign of deterioration perform a CXR and treat patient accordingly.

Specimen Storage:

Specimen	Transport/storage conditions*	Until
Lung Aspirate	≤24 h, 4°C (≤2 h, room temperature)	Inoculation onto culture media and other primary laboratory processing

8. Record Management

1. The signed informed consent is kept in a specified location (either in enrolment documents or in patient file)
2. A note is made documenting the procedure in patient notes
3. Pre and post observation vital signs are recorded in a dedicated observation log.

9. Quality Assurance / Quality Control

1. Initial training of all staff with roles to play through SOP instruction, bedside observation and supervised conducting of the procedure.
2. Subsequent periodic refresher training and observation by trainers
3. Monitoring of laboratory isolation rates and contamination rates

10. References

Scott J, Hall A. The value and complications of percutaneous thoracic lung aspiration for etiologic diagnosis of community-acquired pneumonia. Chest 1999;116:1716-32.

Readon C Ideh , Stephen RC Howie , Bernard Ebruke , Ousman Secka, Brian M Greenwood
 Richard A Adegbola, Tumani Corrah. Use of Percutaneous Transthoracic Lung Aspiration for the Etiologic Diagnosis of Pneumonia – A 25 Year Experience from The Gambia. Int J Tub Lung Dis 2011 Jun;15(6):729-35. Epub 2011 Apr 7



► **Standard Operating Procedure** ◀

Section: Clin Epi

Version: FINAL

Initials: KB

Title: Nasopharyngeal and Oropharyngeal Swabs

Revision Date: 3 April 2012

1. Definitions

- NP = nasopharyngeal
- OP = oropharyngeal
- PCR = polymerase chain reaction
- VTM = viral transport media
- STGG = skim milk tryptone-glucose-glycerin
- PPE = personal protective equipment

2. Purpose / Background

- 2.1. The purpose of this SOP is to describe standardized approach to NP and OP specimen collection procedures across all PERCH sites.
- 2.2. Two NP swab specimens and one OP swab specimen will be collected from each participant for detection of viral and bacterial respiratory pathogens. One NP swab and the OP swab will be placed in VTM for PCR testing. The second NP swab will be placed in STGG for bacterial culture.

3. Scope / Applicability

- 3.1. This SOP is intended for PERCH study staff with a role in NP and OP specimen collection. This includes clinicians, nurses, and clinical and laboratory personnel involved in specimen collection or processing.

4. Prerequisites / Supplies Needed (for each participant)

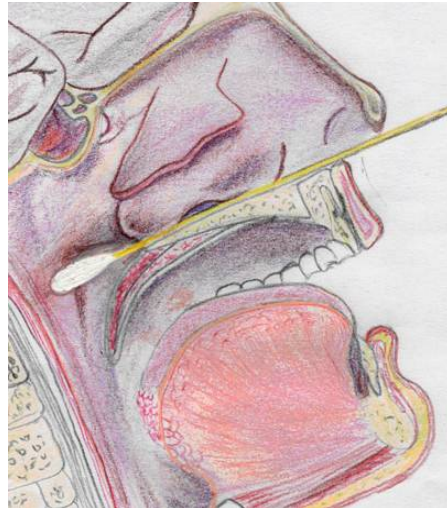
- 4.1. Flocked swabs (2)
- 4.2. Rayon swabs (1)
- 4.3. Tongue depressor (for OP swab)
- 4.4. Vial with VTM
- 4.5. Vial with STGG media
- 4.6. Scissors
- 4.7. Disposable gloves
- 4.8. Surgical mask
- 4.9. Goggles or face shield
- 4.10. Specimen transport bag/container with ice
- 4.11. Specimen label and form
- 4.12. Tissues

5. Roles / Responsibilities

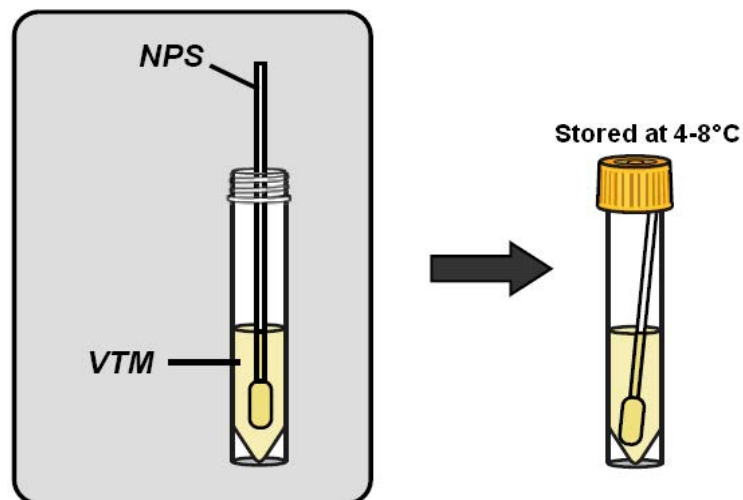
- 5.1 A study nurse (or clinician) is responsible for collecting specimens and ensuring all vials are labeled appropriately. The nurse should also maintain a sufficient inventory of these items at the location where NP and OP swabs are collected.
- 5.2 A laboratory technician is responsible for maintaining sufficient supply of specimen collection materials at the laboratory.

6. Procedural Steps

- 6.1 Timing
 - 6.1.1 NP and OP swabs should be collected as soon as possible after enrollment and ideally before antibiotics are administered.
 - 6.1.2 The NP swab for VTM should be collected first, followed by the OP swab. Both swabs will be placed in the same vial of VTM. The second NP swab should be collected and placed in the STGG vial.
- 6.2 Safety requirements and PPE
 - 6.2.1 Wear disposable gloves and change gloves after each patient
 - 6.2.2 Wash or sanitize hands before putting on and after removing gloves
 - 6.2.3 Wear a surgical mask to minimize exposure to infection during specimen collection
 - 6.2.4 Follow standard precautions and any additional precautions specific to the setting or patient
 - 6.2.5 Dispose of all contaminated waste (gloves, paper, swab handles, etc.) into biohazard waste bags for disposal
- 6.3 NP swab number 1 (flocked swab)
 - 6.3.1 Explain the procedure to the parent and participant. It is expected that the child may shed tears and may try to withdraw from the swab. Emphasize the importance of remaining still during specimen collection to minimize discomfort. Rarely, the NP swab procedure may cause a small amount of bleeding and this can make the swab appear blood-tinged.
 - 6.3.2 Position child on parent/guardian's lap. The parent/guardian should use one arm to hold the child's arms and the other arm should be placed on the child's forehead. They may sit chest to chest for smaller children. If they are sitting chest to chest, the child's head should be positioned over one of the parent's shoulders, and the parent should have one hand on the child's head and the other arm across their back. Study personnel may hold the child at the request of the parent/guardian.
 - 6.3.3 Tilt the patient's head back at a 70 degree angle (see figure below).

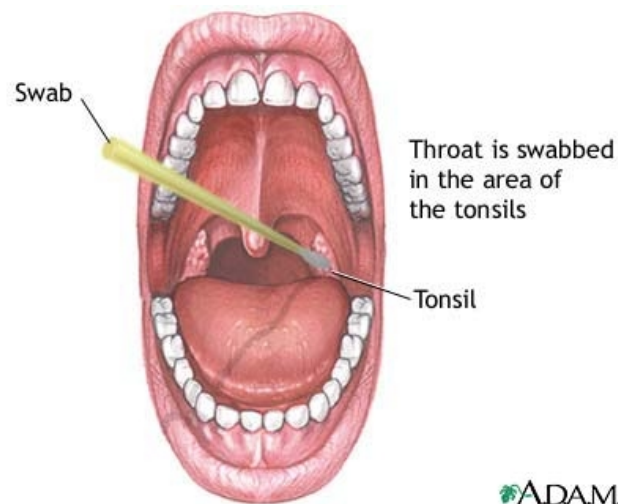


- 6.3.4 Remove the flocked swab from its protective package
- 6.3.5 Insert the swab into one nostril horizontally (not upwards) and continue along the floor of the nasal passage for several centimeters until reaching the nasopharynx (resistance will be met). The distance from the nose to the ear gives an estimate of the distance the swab should be inserted.
- 6.3.6 Do not force the swab. If obstruction is encountered before reaching the nasopharynx, remove the swab and try the other side.
- 6.3.7 Rotate the swab gently through 180 degrees to make sure adequate specimen is obtained. Leave the swab in place for 2-3 seconds to ensure absorbance of secretions.
- 6.3.8 Remove swab and immediately place into vial with VTM by inserting the swab at least ½ inch below the surface of the media. Cut the excess swab handle to fit the transport medium vial and reattach the cap securely.



- 6.3.9 Carefully label specimen with patient ID number, date and time of specimen collection.

- 6.3.10 Complete specimen tracking log with patient ID number, date and time of specimen collection.
- 6.3.11 Place specimen in cool box on ice. Transfer specimen with tracking log to the laboratory as soon as possible.
- 6.4 Oropharyngeal swab (Rayon swab)
 - 6.4.1 For infants, hold the head still, with assistance from parent, and gently open the mouth using a tongue depressor. For older children, ask the patient to open his/her mouth and say 'ahhhhhh'.
 - 6.4.2 Press the outer two-thirds of the tongue down with a tongue depressor, making the tonsils and the posterior wall of the throat visible.
 - 6.4.3 Insert rayon swab, avoiding touching the teeth, tongue, or the depressor.
 - 6.4.4 Rub the swab over both tonsillar pillars and posterior oropharynx. This will cause the patient to gag briefly.
 - 6.4.5 Place the swab into the vial containing VTM (same vial as the first NP swab)
 - 6.4.6 Cut the excess swab handle to fit the transport medium vial and reattach the cap securely.
 - 6.4.7 Carefully label specimen with patient ID number, and date and time of specimen collection.
 - 6.4.8 Complete specimen tracking log with patient ID number, date and time of specimen collection.
 - 6.4.9 Place specimen in cool box on ice. Transfer specimen with tracking log to the laboratory as soon as possible.



- 6.5 Nasopharyngeal swab number 2 (flocked swab into STGG media)
 - 6.5.1 Follow specimen collection procedures for NP swab number 1
 - 6.5.2 Place the swab into the vial containing STGG:
 - 6.5.3 Insert swab to the bottom of the STGG medium in thawed (room temperature) tube.
 - 6.5.4 Raise the swab slightly and cut the wire portion (i.e., the shaft, or using a disinfected scissor) of the swab at the top level of the container. Allow the bottom

portion of the swab (i.e., the tip) to drop into the tube. Discard the remaining shaft into disinfectant solution or a sharps container.

6.5.5 Tighten the screw-cap top securely.

Specimen Transport and Storage:

Specimen	Transport/storage conditions*	Until
NP/OP swabs in Viral Transport Medium	≤24 h, 4°C (≤2 h, room temperature)	Freezing (-70°C)
NP swab in STGG	<8 h, 4°C	Freezing (-70°C)

7. Record Management

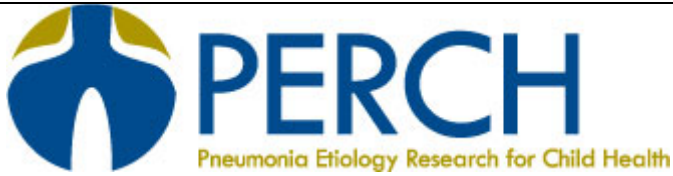
- 7.1. The most recent version of this SOP must be maintained in PERCH study binder at the sites where enrollment occurs and at the office of the study coordinator. All study field staff should have ready access to the SOP.

8. Quality Assurance / Quality Control

- 8.1. All study nurses and field workers will be trained in this SOP. All nurses that will collect specimens will also undergo practical training for NP and OP swab collection. Study personnel will not be approved to collect NP and OP swabs until their competency has been assessed by a supervising clinician and signed off in the training log.
- 8.2. Refresher training will be conducted every 6 months at which time study staff will be required to demonstrate proficiency at NP and OP swab collection.

9. References

- 9.1. Standards: Regulatory references listed
- 9.2. Other SOPs listed. NP and OP swab SOPs from the following settings were referenced: U.S. CDC (China CDC/IEIP collaboration), University of Pittsburgh, KEMRI-Wellcome Trust Collaborative Research Unit, RMPRU, Johannesburg, South Africa
- 9.3. Supplementary Documents: None



► **Standard Operating Procedure** ◀

Section: Clin Epi

Version: FINAL

Initials:

Title: Specimen Collection, Transport, and Storage Algorithm

Revision Date: 4/27/2011

1. Definitions

1.1 VTM: Viral Transport Medium

1.2 STGG: Skim milk, Tryptone, Glucose, and Glycerin medium

2. Purpose / Background

2.1. The purpose of this SOP is to provide overview guidance for the collection, transport and storage of PERCH study specimens from cases and controls. Specific specimen collection SOPs should be consulted for each individual procedure.

3. Scope / Applicability

3.1. This SOP applies to all clinical personnel involved with the collection of specimens from enrolled cases and controls, and to personnel responsible for the transport of specimens from the clinic to the laboratory.

4. Prerequisites / Supplies Needed

4.1. See specimen specific SOPs for supplies needed. Specimen collection SOPs should be referred to for the specimen collection methods.

5. Roles / Responsibilities

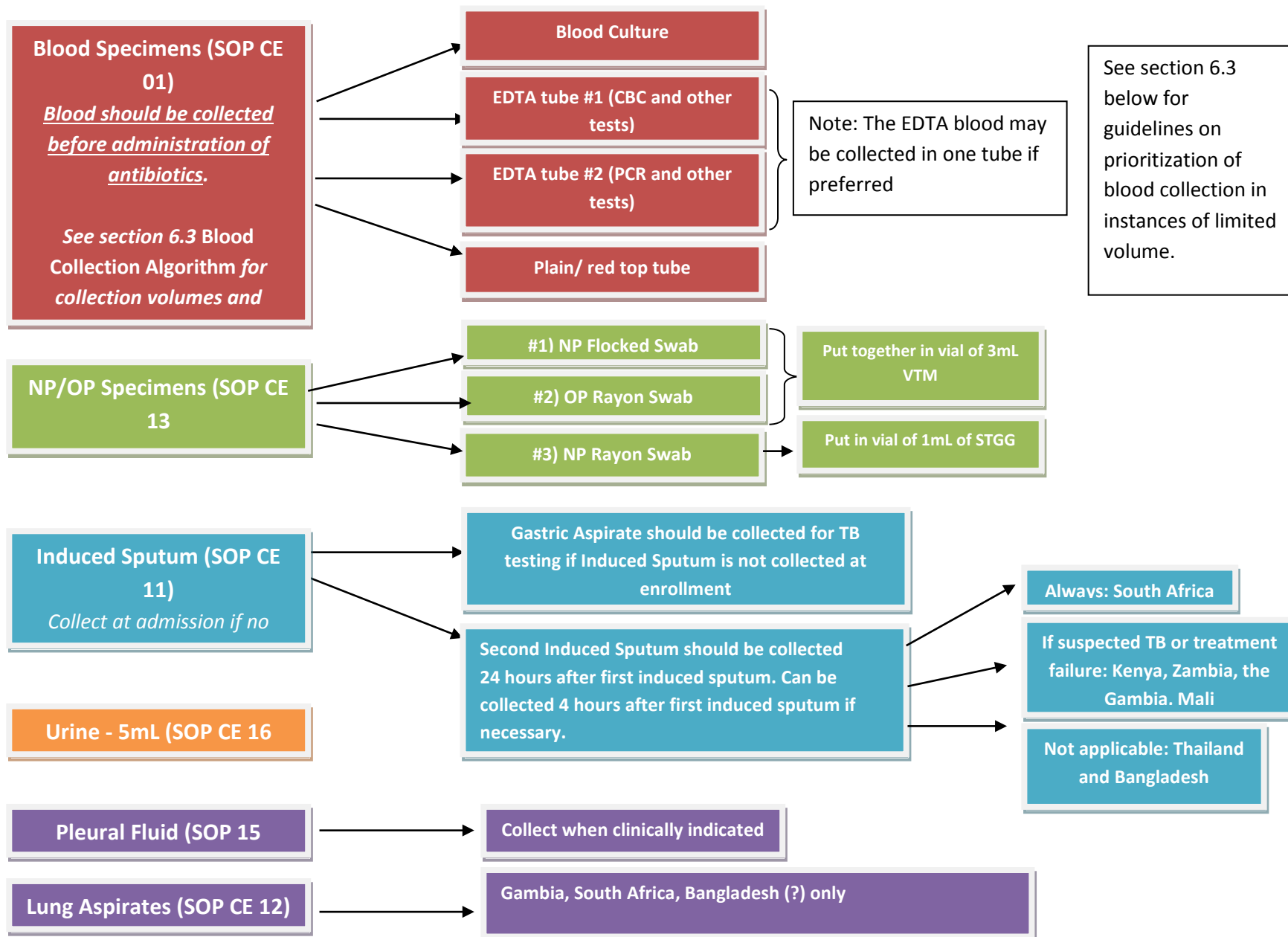
5.1. Clinicians are responsible for following the specimen collection algorithms outlined below for each enrolled case and controls. Specimens should be collected, stored and transported according to the methods described in the individual specimen collection SOPs. Specimen collection CRFs should be completed by a clinician for each specimen that is collected.

6. Procedural Steps

6.1 Study specimens should be collected from each case and control according to the flow charts below

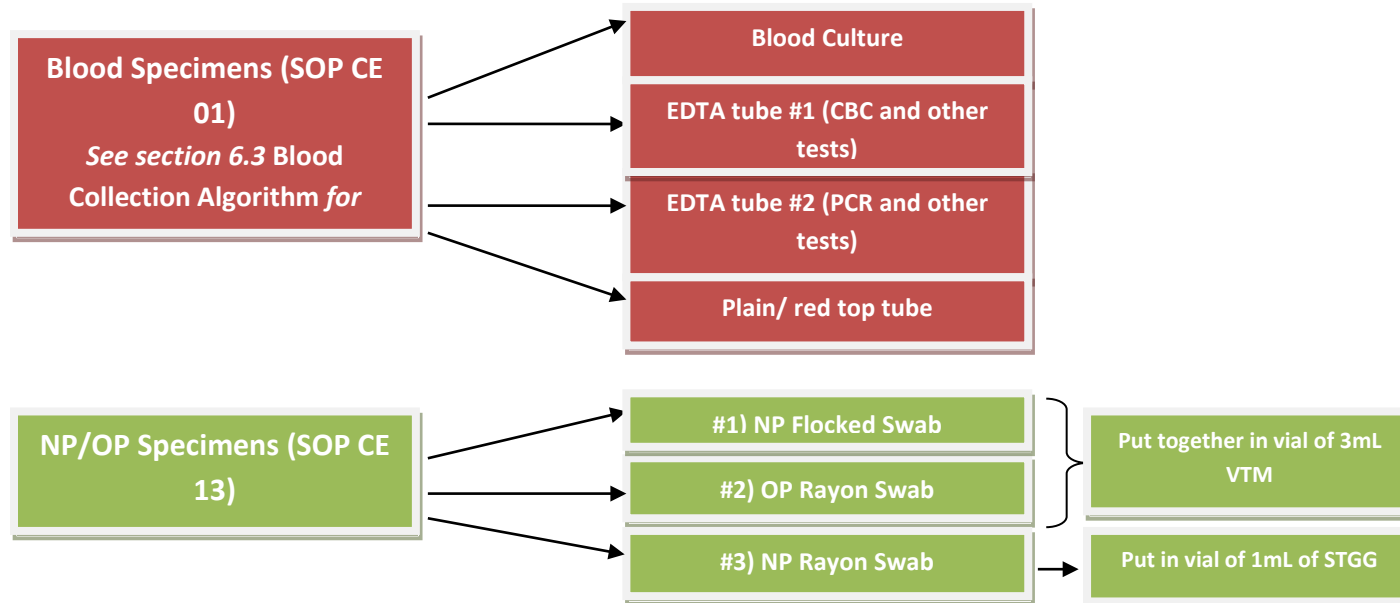
6.1 Enrollment Specimens – Cases

Enrollment specimens should be collected prior to the administration of antibiotics



6.2 MODIFIED PROTOCOL Enrollment Specimens – Cases

If severe pneumonia case defining signs resolve after one dose (children < 2 years) or three doses (children 2-<5 years) of bronchodilator treatment: Continue with study protocol modifying the specimen collection and control enrollment as follows. (See protocol section 4.1.2.)



Do not collect:

1. Induced sputum
2. Lung tap
3. Urine
4. Convalescent sera

6.3 Blood Collection Algorithm

	Clinical Care		Research		
Weight	Blood Culture	EDTA / Purple Top #1 <ul style="list-style-type: none"> • CBC • Malaria • HIV • Sickle Cell 	EDTA / Purple Top #2 <ul style="list-style-type: none"> • Pneumo PCR • Other PCR • Storage 	Plain / Red Top Tube <ul style="list-style-type: none"> • Serology • Biomarkers • Storage 	Total
1- kg	1 ml	0.5 ml	1 ml	0.5 ml	3 ml
2- kg	2 ml	0.5 ml	1 ml	1 ml	4.5 ml
≥3- kg	2 ml	0.5 ml	1.5 ml	1 ml	5 ml

In other words:

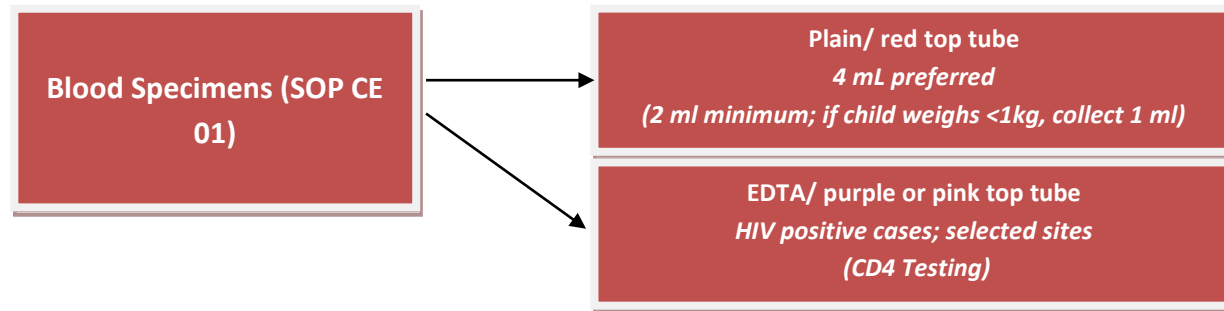
1. Blood cultures (1-2 ml)*
2. CBC, HIV ± malaria, sickle cell (~0.5 ml)
3. Divide the remainder equally into purple and red tops (with at least 1 ml in purple top)*

*Noting maximum blood volumes for weight

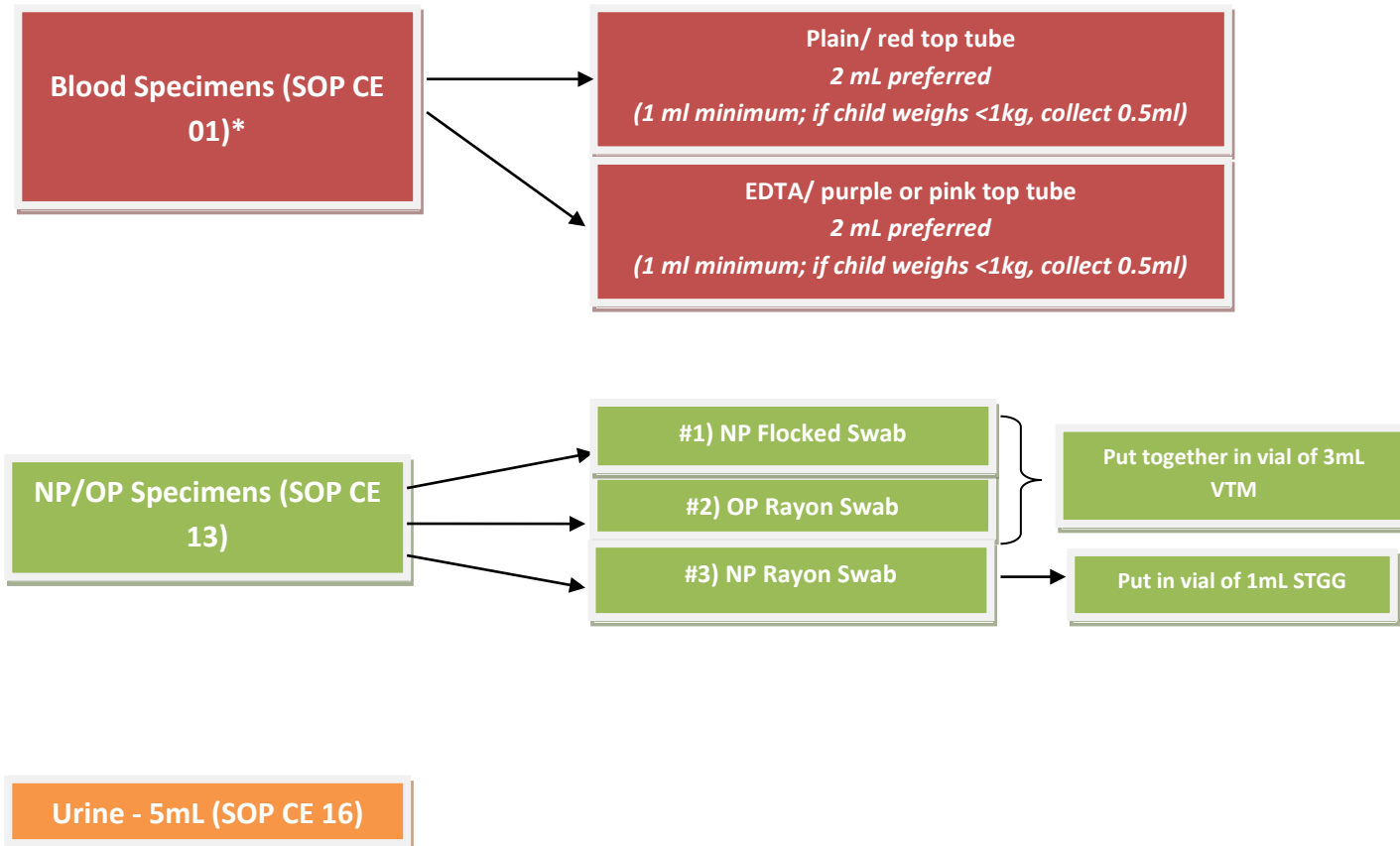
Priorities in instances of limited volume:

1. Blood cultures
2. CBC
3. Malaria slides (for endemic sites)
4. HIV serology (for high prevalence sites)
5. Purple top tube for PCR, etc., (up to 1 ml max.)
6. If there is sufficient volume, any remaining blood should be placed in the red top tube

6. 4 Follow up Specimens – Cases
Collect at 30 day follow up visit (21-90 day window)



6.5 Enrollment Specimens – Controls



*Venous blood is the preferred specimen and should be collected from controls whenever possible. A dried blood spot should be collected ONLY in instances where venous blood collection is attempted and refused by the parent.

6.6 Specimen Transport and Storage Conditions

Below are the conditions under which each specimen must be maintained until it reaches the laboratory for processing. The maximum time a specimen may be stored before processing is also described here. It is the responsibility of the clinical personnel to ensure that specimens are maintained at the proper conditions before reaching the laboratory.

Specimen	Transport/storage conditions*	Until
Blood culture	≤24 h, room temperature or according to manufacturer's instructions	Placement in blood culture machine
Whole blood (EDTA and plain tubes)	<3 days, 2-8°C	Specimen separation
Urine	≤24 h, 2-8°C (≤2 h, room temperature)	Freezing (-70°C)
NP/OP swabs in Viral Transport Medium	≤24 h, 2-8°C (≤2 h, room temperature)	Freezing (-70°C)
NP swab in STGG	<8 h, 2-8°C	Freezing (-70°C)
Induced Sputum	≤24 h, 2-8°C (≤2 h, room temperature)	Inoculation onto culture media and other primary laboratory processing
Lung Aspirate	≤24 h, 2-8°C (≤2 h, room temperature)	Inoculation onto culture media and other primary laboratory processing
Gastric Aspirate	≤24 h, 2-8°C (≤15 min, room temperature)	TB culture
Pleural Fluid	≤24 h, 2-8°C (≤2 h, room temperature)	Inoculation onto culture media and other primary laboratory processing
Lung Tissue	≤24 h, 2-8°C (≤2 h, room temperature)	Inoculation onto culture media and other primary laboratory processing

7. Record Management

n/a

8. Quality Assurance / Quality Control

- 8.1 The responsible clinician must sign each specimen collection CRF
- 8.2 The study coordinator should ensure that all specimens are collected from each enrolled case and control.

9. References

- 9.1 The Pneumonia Etiology Research for Child Health (PERCH) Study Protocol Version 1.0



► **Standard Operating Procedure** ◀

Section: Clin Epi

Version: FINAL

Initials: _____

Title: Pleural Fluid

Revision Date: January 15, 2010

1. Definitions
2. Purpose / Background
 - 2.1. The purpose of this SOP is to describe the procedure for insertion of a needle into the pleural space to allow drainage of fluid.
 - 2.2. Thoracentesis can be performed for diagnosis or therapeutic purposes.
 - 2.3. Thoracentesis is contraindicated in the following clinical settings
 - 2.3.1. Coagulopathy or thrombocytopenia
 - 2.3.2. Hemodynamic or respiratory instability (unless therapeutic thoracentesis is required for management of instability)
3. Scope / Applicability
 - 3.1. This SOP is intended for clinical staff with a role in thoracentesis.
4. Prerequisites / Supplies Needed
 - Sterile drapes and towels
 - Gauze dressings
 - Iodine- or chlorhexidine-based antiseptic
 - Sterile specimen container
 - Sterile instrument tray and instruments (forceps, scissors, needle holders)
 - Suture
 - Sterile blade
 - 18-to-22 Gauge needle (or angiocath)
 - 10 cc syringe
 - 30-60 cc syringe (optional, for aspiration of fluid)
 - Suction apparatus (optional, if chest tube is being placed)
 - Sterile gloves
 - Sterile occlusive dressing
 - Ultrasound machine (if available, for localization of fluid collection)
5. Roles / Responsibilities
 - 5.1. A clinician is responsible for performing this procedure, collecting specimens, and ensuring specimens are properly labeled. A nurse is responsible for assisting with this procedure.
6. Procedural Steps
 - 6.1. Explain the procedure to the parent/guardian/patient and obtain verbal consent.
 - 6.2. Document baseline vital signs
 - 6.3. Sedate the patient, if clinically indicated
 - 6.4. Safety requirements and PPE

- 6.4.1. Wear disposable sterile gloves
 - 6.4.2. Wash or sanitize hands before putting on and after removing gloves
 - 6.4.3. Dispose of all contaminated waste appropriately
 - 6.5. Position patient
 - 6.5.1. Generally the procedure is performed with the patient supine. In cooperative patients, the procedure may be performed with the child seated leaning over a bedside table.
 - 6.6. Identify needle insertion sites: Posterior in the mid-thorax line (if patient in seated position) or mid-axillary line (if patient in lateral recumbent position) at least one rib-space below the level of the effusion. The anterior superior approach (2nd intercostal space at mid-clavicular line) is occasionally necessary.
 - 6.7. Sterilize the area of the chest well planned for needle insertion, guided by dullness to percussion and imaging (CXR or ultrasound, if available)
 - 6.8. Inject local anesthetic
 - 6.9. Insert needle over top of the rib and withdraw fluid. Needle thoracostomy without subsequent tube thoracostomy may suffice if the procedure was performed for diagnostic purposes only or if the procedure achieves sufficient fluid removal to alleviate the child's symptoms and re-accumulation of fluid is considered unlikely.
 - 6.10. Once fluid is aspirated, remove the needle or proceed to insert a chest tube (see appropriate SOP for chest tube insertion)
 - 6.11. Cover the site with a sterile occlusive dressing
 - 6.12. Obtain a post-procedure CXR
7. Record Management
 - 7.1. The most recent version of this SOP must be maintained in the PERCH study binder on the wards and in the office of the study coordinator.
 8. Quality Assurance / Quality Control
 - 8.1. All clinical staff performing this procedure must be trained in this SOP.
 9. References
 - 9.1. Standards: Regulatory references listed
 - 9.2. Other SOPs listed: None
 - 9.3. Supplementary Documents: None



► Standard Operating Procedure ◀

Section: Clin Epi

Version: FINAL

Initials: ADL

Title: Urine Collection

Revision Date: 28 Mar 2013

1. Definitions

- mL = milliliters

2. Purpose / Background

- 2.1. Urine collection is collection of an adequate sample of a child's urine secretion.
- 2.2. Undertaken in a child with clinical evidence of pneumonia, whenever possible (we anticipate that some children will not be able to produce a urine specimen).

3. Scope / Applicability

- 3.1. The SOP will be utilized by the clinic research staff including medical doctors, nurses and physiotherapists
- 3.2. Urine will be collected from all children who can produce a specimen.

4. Prerequisites / Supplies Needed

4.1. Prerequisites

- The procedure will be performed by a nurse, clinical officer, or medical officer. Field workers may assist with this procedure.

4.2. Supplies needed:

- 4.2.1. Clean, screw-top specimen transport containers ("universal" containers are often used)
- 4.2.2. Gauze pads
- 4.2.3. Soap and clean water (or normal saline) if possible.
- 4.2.4. Labels and indelible marker pen.

5. Roles / Responsibilities

- 5.1. Clinical staff – nurse, doctor or physiotherapist will perform all aspects of the procedure.

6. Procedural Steps

- 6.1.1. Give the patient clear instructions to pass urine for a few seconds, and then to hold the cup in the urine stream for a few seconds to catch a mid-stream urine sample. This should decrease the risk of contamination from organisms living in the urethra.
- 6.1.2. To decrease the risk of contamination from skin organisms, the patient should be directed to avoid touching the inside or rim of the plastic cup with the skin of the hands, legs or external genitalia.
- 6.1.3. Tighten the cap firmly when finished.
- 6.1.4. For hospitalized or debilitated patients, it may be necessary to wash the external genitalia with soapy water to reduce the risk of contamination. If soap and clean water are not available, the area may be rinsed with normal saline. Dry the area thoroughly with gauze pads before collecting the urine.
- 6.1.5. Urine collection bags may be necessary for infants. If used, transfer urine from the urine bag to specimen containers as soon as possible to prevent contamination with skin bacteria. Use a disposable transfer pipette to transfer the urine.
- 6.1.6. Label the specimen containers.

6.2. Handling and transport

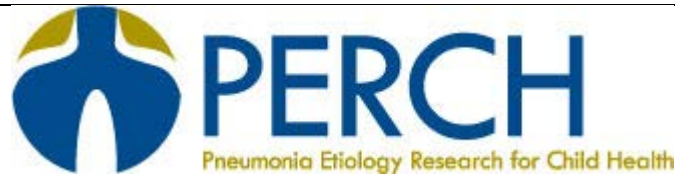
- 6.2.1. Transport to the laboratory within 2–3 hours of collection. If this is not possible, do not freeze but keep the specimen refrigerated at 4–8°C. Keeping the specimen refrigerated will decrease the risk of overgrowth of contaminating organisms.
- 6.2.2. Ensure that transport containers are leak-proof and tightly sealed

7. Record Management

7.1. A case specimen collection form must be complete recording date of collection, time of collection and reason for urine not being collected.

8. Quality Assurance / Quality Control

- 8.1. **References:** Taken from <http://www.who.int/infectious-disease-news/IDdocs/whocds200317/8collection.pdf>



► Standard Operating Procedure ◀

Section: Specimen Collection

Version No. 1.1

Initials: NB

Title: Breath Sound Collection

Revision Date: 15/Apr/2011

1. Definitions

1.1. Abbreviations

- ALRI: acute lower respiratory tract illness

2. Purpose / Background

- 2.1. Chest auscultation is a core component of the clinical exam, yet it has not been incorporated into current algorithms for ALRI management due to difficulties in using standard terminology and obtaining consistent and reliable interpretations.
- 2.2. This project aims to collect breath sound recordings at enrollment from a subset of case and control children enrolled in PERCH to build a sound library that can be used to help standardize breath sound classification and develop better methods for reproducible interpretation.
- 2.3. This project will focus on chest auscultation performed on admission, correlating these findings with other initial diagnostic data. It will not examine changes in breath sounds over time, or in response to treatment.
- 2.4. The Standard Operating Procedure (SOP) is necessary to ensure that breath sound collection is carried out in a standard and reproducible way.

3. Scope / Applicability

- 3.1. This SOP will be utilized by clinic research staff who have been trained in the digital auscultation procedure, including medical doctors and nurses.
- 3.2. Whenever possible, this procedure should be integrated within the standardized physical assessment performed at enrollment. Otherwise, recordings should occur as closely as possible to the time of enrollment, so that breath sounds can be optimally correlated with other clinical data obtained at that time.
- 3.3. Breath sounds will be recorded in a subset of case patients selected using a sampling method developed by each site, for example by obtaining recordings on all cases on specific days of the week. This method can be inserted in each site's specific SOP. The goal will be to obtain recordings from roughly 20-25% of enrolled cases.

3.4. In addition, each site is requested to record breath sounds from 10 control subjects to provide a comparison group with normal findings.

3.5. Contraindications: Refusal of patient or parent/legal guardian.

4. Roles / Responsibilities

- 4.1. A limited number of staff will be trained on this procedure based upon interest and practicality, as determined by the sites. These individuals will be responsible for collecting the sound recordings onto the voice recorder and documenting this collection on the appropriate case report forms.
- 4.2. Each site will need to assign a coordinator. This person should be interested in the topic, comfortable with the electronic devices, and willing to take “ownership” of the project for the site. He or she will be responsible for:
 - 4.2.1. Reading the product manuals and monitoring the safety and function of the equipment.
 - 4.2.2. Developing, along with the site PI, the best method for selecting subjects at their site (see section 3.3), assign personnel according to this schedule, and monitor that the schedule is followed correctly.
 - 4.2.3. Uploading and securely maintaining the data on the site’s designated computer.
 - 4.2.4. Performing local quality control procedures.
 - 4.2.5. Coordinating transfer of data to the Data Coordinating Center.
 - 4.2.6. Reporting quality indicators to the site’s QA coordinator and serving as the main point of contact for the site with the PERCH core team regarding this activity.

5. Prerequisites / Supplies Needed

5.1. Prerequisites

- 5.1.1. This procedure needs to be undertaken in a quiet environment, as appropriate and practical.
- 5.1.2. The procedure should only be carried out by trained, designated study staff.
- 5.1.3. Consent for this procedure is included in the general consent for enrollment in the overall study.
- 5.1.4. The child should be calm and cooperative, as necessary for routine chest auscultation.
- 5.1.5. According to the manufacturer, when in patient contact, the stethoscope should not be connected to any equipment that are “mains-powered”. In other words, the stethoscope and voice recorder must be

on battery power, and the stethoscope should not be used on a patient if it is connected to a charging iPod or a laptop connected to a LAN, AC power supply, or AC-powered peripheral.

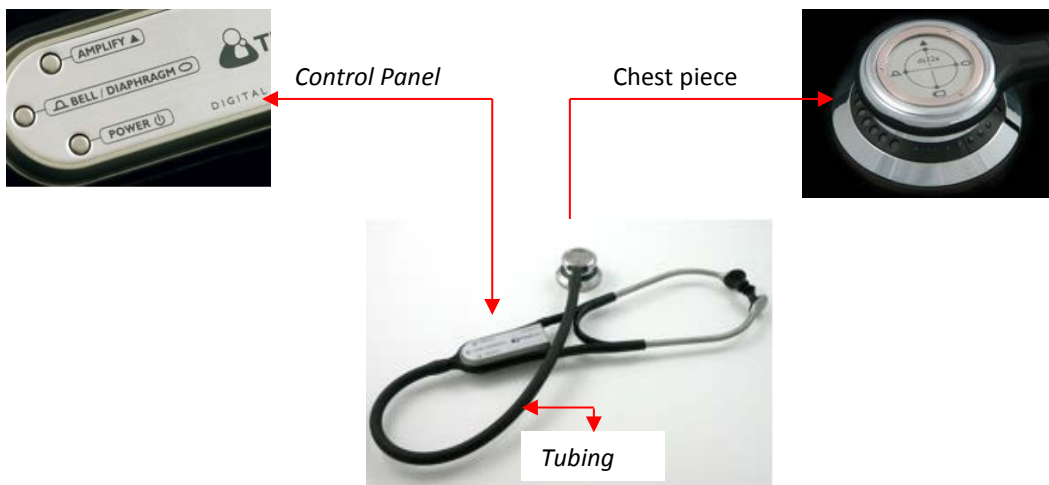
5.2. Equipment needed

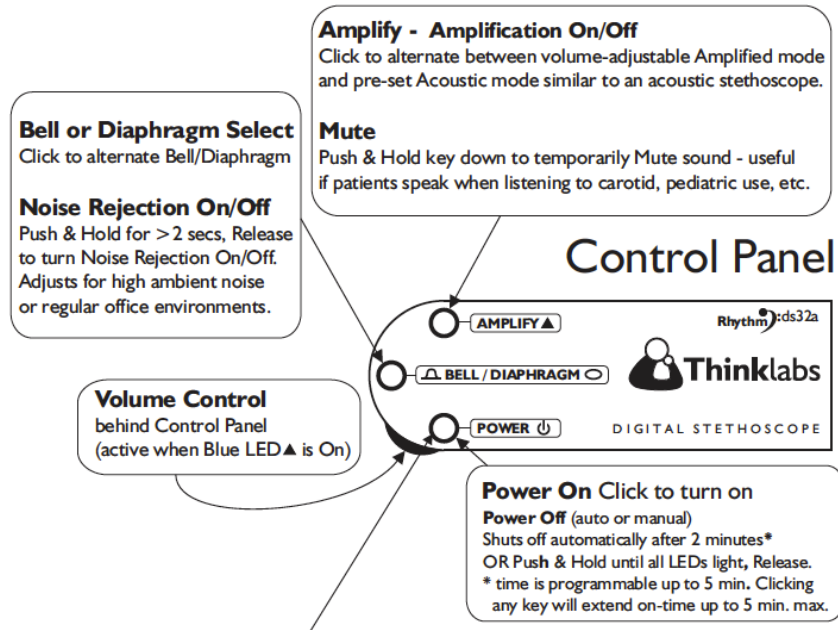
5.2.1. All equipment should be kept in a secure location when not in use. The coordinator must monitor where the equipment are located at all times. Instruction manuals and accessories should be kept accessible. It is strongly recommended to keep the voice recorder, headphones, male to male recording cable and USB connection cable together in a small bag, which should be kept with the stethoscope

ThinkLabs ds32a digital stethoscope	2 will be provided to each site
Sony ICD-UX71 Voice Recorder	2 will be provided to each site
6 AAA batteries (2 for each stethoscope and 1 for each voice recorder)	A minimum of 12 spare batteries should always be kept on hand
Male-Male 2.5mm-3.5mm recording cable	Connects stethoscope to voice recorder
USB connection support cable	Connects voice recorder to computer (you can also connect the device directly to the USB port on the computer)
Headphones	Included with the voice recorder
Computer	It is preferable to save files to one designated desktop computer located in a secure room. All devices are compatible with PC (Windows XP SP2 or higher, Vista, or 7) or Mac (OS X v 10.2.8 or higher) systems.

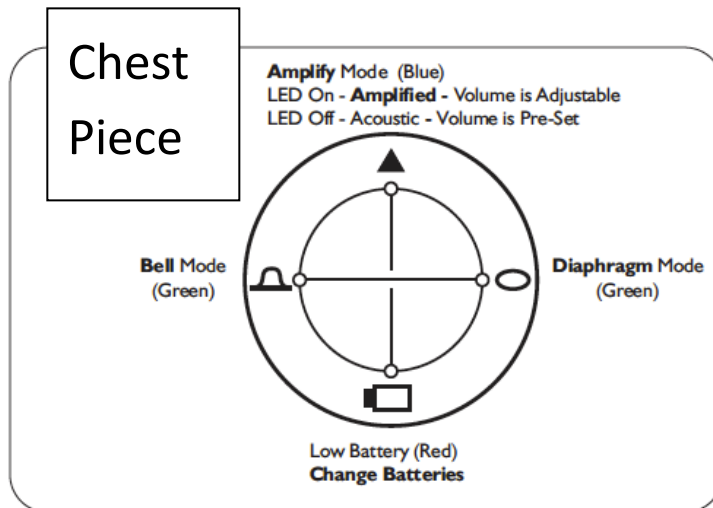
6. Initial Setup

6.1. Digital Stethoscope



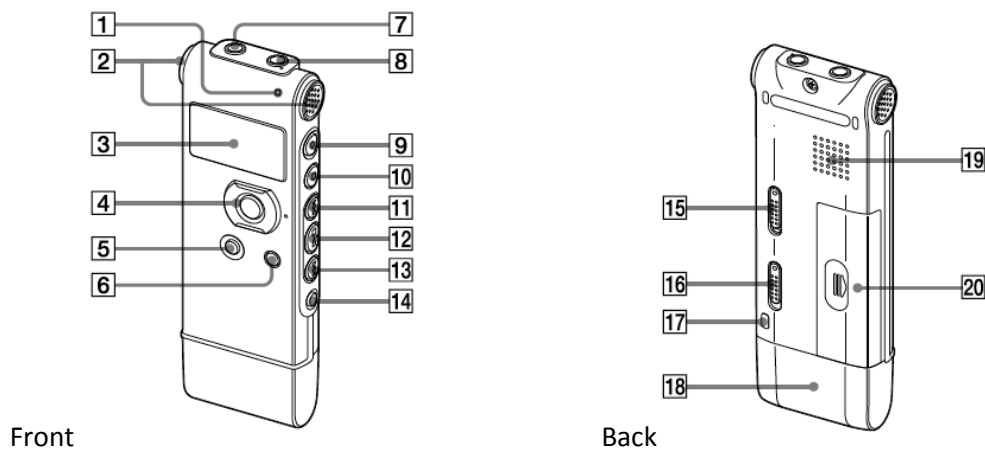











- 6.1.1. Open the back of the control panel and insert 2 AAA batteries.
- 6.1.2. Check that the Low Battery light is not on (red light).
- 6.1.3. Put the stethoscope earpieces into the ears. Turn power on by pushing the POWER button on the control panel. Blue and green LED lights on the chest piece will light up to confirm that the device has been turned on.



- 6.1.4. Using the BELL/DIAPHRAGM toggle button on the stethoscope control panel, ensure that the DIAPHRAGM mode is selected (green light is on next to DIAPHRAGM on the chest piece) (default is BELL).
- 6.1.5. Using the AMPLIFY button on the stethoscope control panel, ensure that the AMPLIFY mode is on (blue light is on below the arrow sign on the chest piece).
- 6.1.6. Adjust the stethoscope volume control to maximum (10) (located on the side of the control panel below the POWER button, see "Control Panel" diagram above.) The volume control is active only when the AMPLIFY blue LED is on.
- 6.1.7. If you hear ambient noise, press and hold the green "BELL/DIAPHRAGM" button that is located on the control panel for more than 2 seconds to switch noise rejection mode on. You will know that the noise rejection mode is on when you hear less ambient noise.
- 6.1.8. The stethoscope automatically shuts off after 2 minutes of inactivity. To extend this to 5 minutes, click the Power key 5 times.
- 6.1.9. These settings can be saved, so that they will be the same each time the stethoscope is turned on. To save these settings, hold the Power key down for 10 seconds. After the first 5 seconds, the red LED light (Low battery indicator) on the chest piece will begin to flash slowly. After 10 seconds, the red LED will flash more quickly, indicating that these preset modes have been programmed. Release the Power button and the device will turn off. Press the Power button once more to turn the device back on again.

6.2. Voice Recorder



- 1 Operation indicator (17, 23, 24, 32, 39, 70, 74, 107)
- 2 Built-in microphones (stereo) (23)
- 3 Display window (10)
- 4 Control button*1 (▲, ▼/VOL (volume +, -) /ENT (enter) button
- 5 DIVIDE button (31, 32, 56)
- 6  (folder)/MENU button (23, 39, 59, 60, 82)
- 7  (headphone) jack*2 (23, 25, 39, 40, 47, 48)
- 8  (microphone) jack (33, 35)
- 9  (record/pause) button (23, 25, 30, 33, 36, 38, 64, 89)
- 10  (stop) button (18, 20, 23, 24, 39, 44, 47, 48, 50, 55, 59, 60, 82, 89, 107)
- 11  (cue/fast forward) button (39, 40, 41, 42, 56, 57, 82)
- 12  (play/stop) button (25, 39, 42, 44, 47, 48, 50, 82)
- 13  (review/fast backward) button (25, 39, 40, 41, 42, 56, 57, 82)
- 14  (repeat) A-B button (39, 44)
- 15 HOLD switch (22, 23, 24, 39, 40, 58)
- 16 DPC (SPEED CTRL) switch (45, 64)
- 17 Opening for a handstrap (A handstrap is not supplied.)
- 18 USB cap
- 19 Speaker
- 20 Battery compartment (13)

6.2.1. Open the back panel (#20) and insert 1 AAA battery.

6.2.2. Turn on device by pushing the “HOLD” switch (#15) to the left.

6.2.3. Set the voice recorder clock:

6.2.3.1. You will be asked to set the clock the first time you insert the battery, or if the battery has been removed for more than 3 minutes.

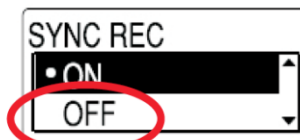
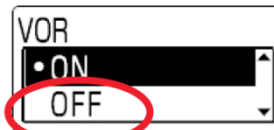
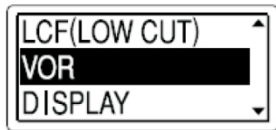
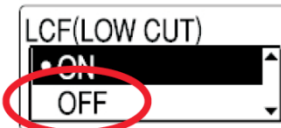
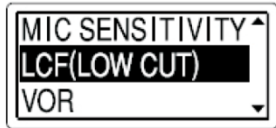
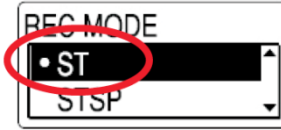
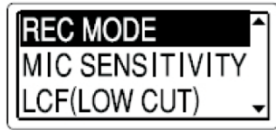
6.2.3.2. Use the up and down arrows to adjust the number, then press ENT (#4) to set and move to the next category. The year will flash first, then the month, day, hour, and minute. After all are set, press the STOP button (#10).

6.2.3.3. The clock can also be set without removing the battery. Press and hold the MENU button (#6) until you see the menu appear. Using the up and down buttons, scroll down to “DETAIL MENU” and press ENT (#4). Use the up and down buttons to scroll down to “DATE&TIME” and press ENT (#4). Then set the date and time as described above.

6.2.4. Push and hold the MENU key (#6) until a beep is heard (about 2 seconds), at which point you stop pressing the button and use the up and down arrows to make the following selections (see figures below). Press the ENT button (#4) each time a selection should be made:

6.2.4.1. Rec Mode (press ENT) -> ST (press ENT)

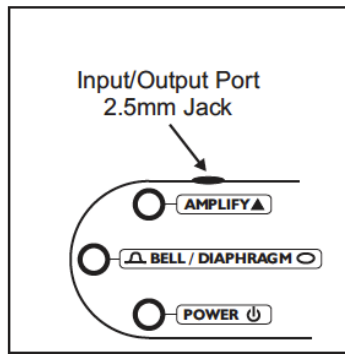
- 6.2.4.2. LCF (low cut) (press ENT) -> Off (press ENT)
- 6.2.4.3. VOR (press ENT) -> Off (press ENT)
- 6.2.4.4. Detail Menu (press ENT) -> Sync Rec (press ENT) -> Off (press ENT)
- 6.2.4.5. Press the MENU button to exit. You will have to press the MENU button twice to exit if you are in the Detail Menu.



7. Procedural Steps:

7.1. Set up stethoscope and voice recorder:

- 7.1.1. Connect the right-angled 2.5mm male to male end of the connecting cable to the jack located on the side of the stethoscope control panel (above the Amplify button).



7.1.2. Connect the straight 3.5 mm end of the connecting cable to the RED microphone jack (#8) at the top of the voice recorder.

7.1.3. As soon as the two devices are connected, choose AUDIO IN on the voice recorder display by pressing the ENT key (#4). (This will happen each time the two devices are re-connected).

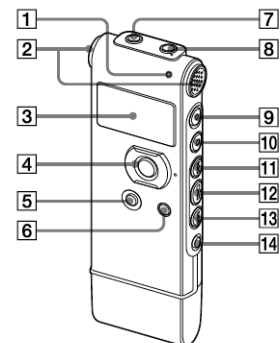
7.2. Recording sounds:

7.2.1. Ensure that the patient is as calm as possible, preferably in the parent’s arms. Position patient for chest auscultation. Ideally, the chest piece should be able to have direct contact with the skin at all six locations described below.

7.2.2. Make sure the stethoscope and voice recorder are both on. If the voice recorder display has turned off (happens automatically after 10 minutes of inactivity) press any button to turn it back on.

7.2.3. Check that the amplify light on the stethoscope is ON and that the volume is turned up to 10 (maximum)

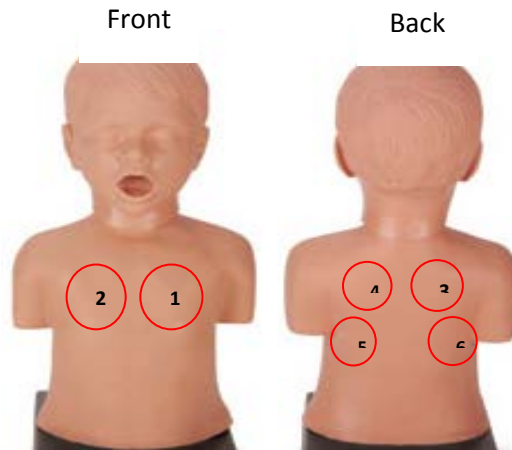
7.2.4. When ready, press the Record button on the voice recorder (#9, top button on side of device, marked with a red circle). The small light (LED) on the upper part of the recorder (#1) will first flash orange, and then steady red to indicate active recording.



7.2.5. After the light turns steady red, speak into the stethoscope chest piece, stating the date and reading out the child’s study ID number. Hold the chest piece close to your mouth and speak LOUDLY. Then, without stopping the recording, begin auscultation.

7.2.6. Record breath sounds at the six designated locations in sequential order (illustrated below), holding for at least 10 seconds at each position. (The respiratory rate timers are useful for timing

each 10 second period). DO NOT stop the recording in between locations. The sequence is: front first, heart side first; then in the back, do the top first and go counter-clockwise. Make sure that the stethoscope is firmly applied directly to the skin, and do not move the stethoscope during the recording.



Order of Auscultation:

- 1 = FTL = Front Top Left
- 2 = FTR = Front Top Right
- 3 = BTR = Back Top Right


- 4 = BTL = Back Top Left
- 5 = BBL = Back Bottom Left
- 6 = BBR = Back Bottom Right

- 7.2.7. After auscultation is complete, press the Stop button on the recorder (#10, below the record button, marked with a square). The small light (LED) on the recorder will flash orange and then turn off. Only one sound file should be produced for each child. The recording should be approximately 70 seconds in length.
- 7.2.8. The file name of the new recording will be on the top line of the recorder display. Each time a recording is made, the file is automatically named in the following format: YYMMDD_XXX, where the last 3 digits are assigned to each file in the order of recording, starting with 001 for each day. Write this number down on the CRF [Form 4], and the Sound Recording Log (see sample log at the end).
- 7.2.9. During the first few times of performing this procedure, the operator should play back the first few seconds of the recording while still with the patient, to check the adequacy of the recording.
 - 7.2.9.1. Headphones, such as those included with the voice recorder, should be used.

- 7.2.9.2. Insert the 3.5 mm end of the headphone cable into the GREEN headphone jack on the voice recorder (#7).
- 7.2.9.3. Ensure that the correct filename is listed at the top of the voice recorder display. If not, see section 9.5 for tips on navigating the sound files.
- 7.2.9.4. Using the + and – buttons on the voice recorder, turn the volume up to maximum (30)
- 7.2.9.5. Push the PLAY button (#12, marked with a triangle and square) and listen that their spoken voice is audible, background noise is not excessive, and that breath sounds for at least the first location have recorded correctly.
- 7.2.9.6. The recording can be paused by pressing the PLAY button again, and stopped by pressing the STOP button (#10).

- 7.3. Turn off the stethoscope by pressing the Power button for a few seconds (or it will turn off automatically), and turn off the voice recorder by pushing the Hold (#15) switch to the right. Disconnect the stethoscope from the voice recorder.
- 7.4. To erase a recording on the recorder itself, first make sure the file you want to erase is displayed. Then press and hold the MENU button (#6) and then use the up and down arrow buttons to scroll down to ERASE A FILE and press ENT (#4). Be careful not to select ERASE ALL. Sound files can also be deleted after transferring them to a computer by dragging them to the Recycle Bin on the computer desktop.

8. Sound file transfer

- 8.1. Designate a single computer at each site for uploading sound files. This computer should be located in a safe and secure location. A new folder should be created for the storage of sound files. These files should be protected by the same or similar back-up procedures as other electronic data collected for PERCH. Ideally, the folder would be located on a secure network drive that is automatically backed up on a periodic basis.
- 8.2. Remove the bottom cap from the voice recorder (#18) to reveal the USB connector.
- 8.3. Insert the USB connector into an appropriate USB port on your computer. (Marked with ). Use the USB connection support cable provided with the recorder if space around the USB port is limited. The recorder should be recognized by the computer without the installation of additional drivers, and will appear as a removable device on the computer directory. The recorder display will say “Connecting”.
- 8.3.1. On a PC system, a window will appear asking “What do you want Windows to do?” Select “Open folder to view files using Windows Explorer,” and a window will appear.
- 8.3.2. On a Mac system, an icon for the device will appear. Click on the icon to open a window.

- 8.4. In the device folder, open the VOICE folder, then FOLDER01, and a list of the files stored on the device will be displayed. Select the files to be copied to the computer and drag them into the designated folder on your computer.
- 8.5. Using the sound recording log, match each sound file (named by date and sequence number) with each subject, and rename the sound file with the matching subject's PERCH case number.
- 8.6. It is not necessary to delete the files on the recorder, as there is space to hold several hours on each recorder, and each file will have a unique name. These files can serve as backup in case the computer files are lost.
- 8.7. To disconnect the voice recorder from a PC computer, left-click the "Safely Remove Hardware" icon in the taskbar, and then click "Safely remove USB Mass Storage Device." On a Mac computer, control-click the device's icon and select "Eject" or drag the icon to the Trash desktop icon. After the LED light on the recorder stops flashing, the device can be removed from the USB port.
- 8.8. Quality Control
 - 8.8.1. Quality control procedures should be performed by the auscultation project coordinator.
 - 8.8.2. As recordings are uploaded, check that the sizes of the files are similar (1.5-2.0 MB).
 - 8.8.3. Periodically listen to a few of the recordings as you upload them.
 - 8.8.3.1. During the first few weeks, at least two recordings should be reviewed from each staff person each time files are uploaded to the computer. Afterwards, at least 2 or 3 recordings overall should be reviewed once a week, or more frequently if there are continued problems with technique.
 - 8.8.3.2. Use the headphones included with the voice recorder to listen to the sound files. These headphones plug into the headphone jack on your computer (see section 7.2.7.2). Click on the sound file to play it. Volume should be set to maximum (a volume control box will appear on your computer screen).
 - 8.8.3.3. Confirm that the study ID spoken in the recording is understandable and matches the PERCH case number, which should also be the name of the sound file.
 - 8.8.3.4. Confirm that the sound volume is adequate, that breath sounds are appropriately captured, and that the level of ambient noise is acceptable.

8.9. Please refer to the Manual of Operations regarding transfer of sound data to the Data Coordinating Center (DCC). Essentially, sound files will be sent together with the digital chest radiograph files on a periodic basis using the same procedure.

8.10. Quality indicators associated with this activity, such as number of patients recorded and number of files transferred to the DCC, will be incorporated in the overall quality assurance plan. The auscultation project coordinator will provide these data to the appropriate person in charge of QA reporting.

9. Troubleshooting and other points

9.1. Problem: The stethoscope turns off too quickly

9.1.1. Unless the settings are programmed as shown in section 6.1.8, the stethoscope will shut off after 2 minutes and revert to default settings when turned back on. If this is the case, repeat steps 6.1.3-6.1.7.

9.2. Problem: No sound is heard when playing back on the recorder

9.2.1. Use the headphones (see section 7.2.7.2).

9.2.2. Adjust the volume of the recorder (right and left sides of the ENT button #4).

9.2.3. Make sure all cables are fully plugged in.

9.3. Problem: Recordings do not seem loud enough

9.3.1. Ensure that the AMPLIFY mode is on (blue light on the chest piece) AND the volume control is set to 10.

9.3.2. Make sure on the recorder that MIC SENSITIVITY is set to HIGH (H) (press and hold MENU key (#6) for 2 seconds and then use the down arrow to highlight MIC SENSITIVITY, press ENT (#4) to select, use the up and down arrows to highlight "HIGH" and then press ENT again to select. Press MENU to exit.)

9.3.3. Check if the battery is low on either device.

9.4. Problem: There is a lot of static or distortion of sound

9.4.1. Do not place a mobile phone, an AC power source, or fluorescent lamp nearby while recording.

9.4.2. Ensure that when the stethoscope cable is plugged into the voice recorder, AUDIO IN is selected

9.5. Problem: Unable to find the correct file on the recorder's display

- 9.5.1. The top line is displaying another category: Using the up and down arrow buttons, the top line of the display cycles between the folder name, message title name, “artist name” (for music files), and file name.
- 9.5.2. The directory is in the wrong folder: There are five folders on the recorder for storing sound files. The current folder is listed at the top of the display, and by default is at FOLDER01. You can move between folders by pressing the MENU key (#6), using the up and down arrows, and then pressing the ENT key (4). Since file management is best performed on the computer, there is no need to move to or store recordings in other folders.
- 9.5.3. The wrong file is displayed: The number of recordings in the folder is indicated at the bottom left corner of the display. The first two digits indicate the record number, the second two digits (after the slash) indicate the total number of files in the folder. E.g., 02/04 means the second file of four. One can move between recordings within a folder using the backward and forward skip buttons on the side of the recorder (#11 and #13).

10. Maintenance

- 10.1. Swab the stethoscope with an alcohol pad for disinfection between patients as per routine practice. Do not immerse in liquid, and do not attempt to sterilize. Do not store above 43C (eg, in a closed automobile in the sun).
- 10.2. The battery should last through approximately 13 hours of recording. Remaining battery life for the voice recorder is indicated by an icon in the lower right corner of the display. An estimated battery life for the stethoscope is not provided. When the battery on the stethoscope is low, a red LED will light up next to the battery icon on the chest piece.

11. Contact information

- 11.1. Questions: contact Niranjan Bhat, MD at nbhat2@jhmi.edu (email), niranjan_bhat (Skype), or 001-410-955-6931 (phone).

