UC San Diego

Altman Clinical and Translational Research Institute

Center for Clinical Research

Clinical Procedures Manual

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Purpose of this Manual

This document, CCR-010: Clinical Procedures Manual, has been created to provide guidance on the standard clinical procedures that are commonly required for research protocol implementation and data collection across study protocols and participants in the Center for Clinical Research (CCR). CCR personnel provide treatment as described in the study protocol and ordered by the study principal investigator. All procedures require a signed order from an authorized provider. No standard of care services will be provided. While the procedures described here are commonly required, all CCR personnel must be aware of and adhere to any certification and/or licensing requirements or limitations imposed by their scope of practice, and are responsible for safely and competently executing any study procedures undertaken with a study participant.

Study participant safety and comfort

All CCR personnel strive to provide a safe, friendly, accommodating, pleasant, and family-focused environment for study participants, family members, legal guardians, and legally authorized representatives. The safety of CCR study participants supersede data collection needs and study procedures.

Responsibilities

Responsibilities of research personnel are addressed in more detail in CCR-009: Research Team Roles and Responsibilities. However, for any research study, the principal investigator (PI), as the leader of the research team, remains responsible for the study and for supervising and ensuring adequate training of any personnel on the study team to whom study tasks are delegated.

Procedures

Anaphylaxis management

Description

Anaphylaxis is a severe allergic reaction to a foreign substance that occurs rapidly and may be fatal if untreated. While anaphylaxis is rare, new medications and biologics carry an associated risk of producing an anaphylactic reaction.

Anaphylaxis often produces signs and symptoms within minutes of exposure to an offending stimulus. Most instances begin within 30 minutes after medication administration, but some reactions might develop later. The clinical signs of anaphylaxis usually involve multiple body systems (cutaneous, respiratory, and cardiovascular). The symptoms of anaphylaxis are varied and, in severe cases, may progress to shock and cardiovascular collapse, characterized by, among other things, eventual loss of consciousness. Fatalities during anaphylaxis usually result from delay in the administration of epinephrine and from severe respiratory complications, cardiovascular complications, or both. **It is important to recognize the first signs and symptoms of anaphylaxis promptly so that treatment can be administered without delay. In general, the sooner the symptom onset, the more rapidly evolving and severe the anaphylactic reaction.**

Clinical presentation

Urticaria and angioedema are the most common manifestations of anaphylaxis, but an array of signs and symptoms is possible (Table 1). Urticaria (hives) are raised, often itchy, wheals on the surface of the skin. Angioedema is a swelling similar to urticaria, but the swelling is beneath the skin rather than on the surface. The swellings, called welts, usually occur around the eyes and lips. They may also be found on the hands, feet, neck and in the throat.

Features of early or mild anaphylaxis may include swelling and hives at the injection site, sneezing, nasal congestion, tearing, coughing, and facial flushing. These symptoms are generally associated with minimal dysfunction.

Features of moderate to severe anaphylaxis include obstructive swelling of the upper airway, hypotension and marked bronchospasm (constriction of the air passages of the lung caused by spasmodic contraction of the bronchial muscles).

Table 1: Frequency of occurrence of signs and symptoms of anaphylaxis	
Signs and symptoms	**Approximate frequency**
Cutaneous	**90%**
Generalized urticaria (hives)and/or angioedema (welts)	85 – 90%
Flushing	45 – 55%
Pruritus (itchiness) with or without rash	2 – 5%
Respiratory	**40 – 60 %**
Upper airway angioedema (stridor)	50 – 60%
Dyspnea (difficulty breathing), wheezing	45 – 50%
Rhinitis (nasal congestion)	15 – 20%
Dizziness, syncope (fainting), hypotension	**30 – 35%**
Abdominal	
Nausea, vomiting, diarrhea, cramping pain	25 – 30%
Miscellaneous	
Headache	5 – 8%
Substernal (chest) pain	4 – 6%
Seizure	1- 2%
From: *The diagnosis and management of anaphylaxis: an updated parameter. (2005). Journal of Allergy and Clinical Immunology, 115, S483-523.*	

Differentiating anaphylaxis from other reactions

Anaphylaxis must be distinguished from fainting (vasovagal syncope), anxiety, and breath-holding spells, which are much more common, yet benign reactions.

Allergic reaction

Allergic reactions exist on a spectrum, the extreme end of which is anaphylaxis. Milder forms may involve the skin, manifesting with urticaria, pruritus, or rhinitis; and/or the respiratory system (sneezing, rhinorrhea, etc.). Anaphylaxis is set apart from simple allergic reactions when there is simultaneous involvement of the cardiovascular system and loss of intravascular volume as well as respiratory obstruction.

Vasovagal reaction/Fainting

During a vasovagal reaction, the participant may suddenly become pale, dizzy, and may lose consciousness and collapse. This is distinguished from an episode of anaphylaxis as there is a lack of hives, itching, stridor, and wheezing. Fainting is sometimes accompanied by brief clonic seizure activity (i.e., rhythmic jerking of the limbs), but this generally requires no specific treatment or investigation. The participant should be placed in a recumbent position and turned on his/her side, with slight pronation. This position will help prevent aspiration and keep the airway open while the participant is unconscious, especially if seizure activity is present.

Recovery of consciousness usually occurs within a minute or two, but the participant may remain pale, diaphoretic and mildly hypotensive for several more minutes**. If altered level of consciousness persists for more than two to three minutes, emergency medical services (EMS) should be activated and treatment for anaphylaxis should be initiated, as a change in level of consciousness may signal hypoxia.**

Injection site reactions

An injection site reaction is a mild local reaction, which resolves by itself within a few minutes. It does not require special observation.

Procedure

I. Before each study visit, and prior to any injectable medication administration by CCR personnel, study participants should be asked about the following:
    i. Known allergies
    ii. Past reactions to medications, biologics, or foods
    iii. Fainting with injections or blood draws
II. Document allergies and/or other reactions in the participant's record.
III. Perform baseline nursing assessment, including vital signs.
    i. If the participant reports having a moderate to severe reaction that may be allergic in nature, or if the participant has reported previous anaphylaxis, document the details of the reported reaction in the participant's record.
IV. Instruct participant about the signs and symptoms of anaphylaxis that require immediate reporting, including:

i. Urticaria
ii. Localized/generalized itching
iii. Shortness of breath, with or without wheezing
iv. Uneasiness and/or agitation
v. Periorbital or facial edema
vi. Lightheadedness/dizziness
vii. Tightness in the chest
viii. Abdominal cramping/nausea
ix. Chills

V. If the study participant develops any sign of an allergic reaction or anaphylaxis, refer to the CCR Anaphylaxis protocol.

Outpatient Infusion Therapy

Purpose:

To outline standardized procedures for the safe, efficient, and consistent administration of outpatient infusion therapy in a clinical setting, ensuring patient safety and protocol compliance.

Scope:

Applies to all clinical staff involved in administering intravenous (IV) therapies to outpatient participants in the infusion clinic, including but not limited to:

- Registered Nurses (RNs)
- Study Coordinators
- Physicians/Principal Investigators (PIs)
- Pharmacy staff
- CRC

Responsibilities:

Licensed Professionals (RNs, LVNs, NP, MD, pharmacist or pharm technician) independently double check Name, DOB, MRN, IRB, Name of the medication, route of administration, rate, flush type and amount, expiration date and time and name of the visit.

- Verify orders and assess the patient prior to infusion
- Prepare and administer the IV therapy
- Monitor the patient throughout the infusion
- Document all observations and interventions

Study Coordinator:

- Confirm visit schedule and protocol requirements
- Ensure informed consent has been signed and documented
- Provide protocol-specific infusion instructions or documentation

Physician/PI:

- Review and sign infusion orders
- The PI or sub-I is onsite and available for first time infusions and/or investigational product administration
- Remain available for adverse reaction consultation

Research Pharmacy:

- Prepare and label investigational or standard medications per OPRX
- Confirm drug stability and expiration

Pre Infusion preparation

I. Verify Order & Documentation
   a. Confirm valid physician's order
   b. Confirm study eligibility (if applicable)
   c. Review patient medical history, allergies, and premeditations
II. Patient Verification
   a. Confirm identity using two patient identifiers
   b. Obtain and document vital signs
III. IV Access
   a. Assess for appropriate venous access
   b. Insert IV catheter using aseptic technique
   c. Document catheter size, site, and number of attempts
IV. Medication Verification
   a. Double-check medication label against the order and protocol
   b. Confirm storage and stability per guidelines
   c. Obtain co-sign from a second nurse if required

Infusion Administration

I. Premedication (if applicable)
   a. Administer premedications as per protocol and document
II. Start Infusion
   a. Start IV infusion at the prescribed rate
   b. Use infusion pump with proper programming
   c. Observe for signs of infiltration, reaction, or discomfort
III. Monitoring
   a. Monitor vitals at baseline, during infusion, and post-infusion per protocol
   b. Immediately report and document any infusion-related reactions
   c. Follow emergency protocol if anaphylaxis or other critical events occur

Post Infusion procedure

I. Flush Line & Remove IV

a. Flush per protocol
b. Remove IV and assess site
c. Apply dressing and document any complications

II. Observation Period
a. Monitor patient for the specified post-infusion period according to protocol
b. Record final vital signs

III. Documentation
a. Infusion therapy record
b. Vital sign log
c. Adverse event report (if applicable)
d. Nursing notes
e. Study-specific Case Report Form (CRF) if applicable

Blood and Specimen Collection

Clinical personnel who are trained[1] to to perform, process, store, and ship blood, bodily fluids, and skin tissue samples will follow all standards, guidelines and universal precautions, including use of required personal protective equipment (PPE) when acquiring and working with blood and tissue from human study participants.

Procedure

I. Prior to specimen collection, confirm study participant identification against study source documents.
II. For venipuncture in children, consider use of local anesthetic.
III. Verify orders and confirm protocol requirements for specimen collection.
IV. Utilize safety collection devices with needle safety shields for all venipunctures and associated blood sampling procedures.
a. When using sponsor- or central lab-provided laboratory kits that do not include needle guards, CCR personnel will utilize CCR stock of venipuncture needles and blood sampling supplies with safety shields.
V. Perform venipuncture[2] or other specimen collection according to orders, study protocol, study laboratory manual, and established procedures.
a. UCSDHP 393.1 Central Venous and Arterial Catheter Management and Care, attachment A specifies appropriate venous catheter care and blood sampling procedures from midline, short-term-dual/triple lumen, introducer venous sheath, peripherally inserted central catheters (PICC)

[1] See CCR-109 WORKSHEET: Personnel Training Documentation for training requirements.
[2] No more than 3 attempts to obtain specimens via venipuncture are permitted by a single provider. Obtain and document participant's verbal assent to undergo additional venipuncture attempts.

non-valved or valved, Hickman (tunneled catheter/non-valved), Groshong (tunneled catheter/valved) and implanted port lines.

b. Per UCSDHP 393.1, perform blood sampling as follows:
   i. Discontinue or stop any infusions
   ii. Aspirate 3-5 ml of blood and discard when drawing from central line.
   iii. Withdraw the specimen using a syringe or vacutainer technique (no vacutainer for valved PICC).
   iv. Flush lumen with 20 ml of normal saline. Re-initiate infusion as indicated

VI. Ensure specimens are properly labeled with codes or identifiers according to protocol and/or local lab requirements.
VII. Transport specimens to lab for prompt processing, shipment, and/or storage.
VIII. Document the details of this procedure in the study file.

CenTrak Monitored Equipment

Requirements

I. The metabolic kitchen refrigerator and laboratory biospecimen refrigerators and freezers (-20°C, -80°C) require continuous monitoring for temperature excursions. These refrigerators and freezers are connected to CenTrak[3] for continuous monitoring, daily temperature recording at 0400 and 1800 hours, and temperature excursion notifications. A CenTrak sensor installed on a refrigerator or freezer sends electronic temperature feeds at least every 5 minutes to a central secured server with intranet-wide remote access. The CCR staff can review the temperature records online at any time.
II. Monitored alarms will sound when a refrigerator or freezer exceeds the specified temperature ranges and send an automated phone call and/or text and email notifications to the senior laboratory technician or designee until a response is received, the temperature returns to the specified range, and/or the alert is acknowledged.
III. The specified monitored ranges for the CCR equipment are as follows:
   a. Metabolic kitchen refrigerator temperature range = 1°C to 3.9°C
   b. Laboratory biospecimen refrigerator temperature range = 2.2°C to 7.8°C.
   c. Laboratory biospecimen freezer temperature ranges:
      i. -20°C = -17°C to -25°C
      ii. -80° C = -65°C to -85°C

Procedure

I. CenTrak monitoring alarms between the hours of 0700 and 1600 work days:
   a. A monitored temperature outside the specified range for 15 minutes will initiate phone call and/or text and email notifications to the senior laboratory technician or designee until a

[3] Laboratory refrigerator and freezers are calibrated and maintained by Frio-Zone.

response is received, the temperature returns to the specified range, and/or the alert is acknowledged. If assistance is needed from facilities, staff can contact the Facilities Maintenance main number.

II. CenTrak monitoring alarms between the hours of 1600 and 0700 and non-work days (e.g., weekends and holidays).
   a. A monitored temperature outside the specified range for 15 minutes will initiate phone call and/or text and email notifications to designated on-call personnel (senior laboratory technician or clinical on-call phone) until a response is received, the temperature returns to the specified range, and/or the alert is acknowledged.

Designee	Phone	Email
On-call phone	858-822-2533	bcale@health.ucsd.edu
Senior Laboratory Technician	858-822-2533	cgroom@health.ucsd.edu
Campus Watch Stander	858-967-2210	Facilities Management
Campus Facilities	858-534-2930	Facilities Management Main

III. The assigned CCR personnel will investigate the discrepancy via the CenTrak website or in person until the situation is resolved, and/or contact the Facilities Management watch stander or designee if the unit is not functioning properly. Facilities Management will inspect the unit to determine the appropriate action, and if necessary, will contact Frio-Zone Refrigeration (619-379-0259) to provide the location and unit details and arrange to meet the Frio-Zone dispatched technician. Specific details to be provided include:
   a. Location
   b. Description of equipment issue
   c. Account Code 637100
   d. PO# 91571152

IV. The primary CCR on-call responder acknowledges the alarm and notifies the medical director.

V. Remediation for unit malfunction or failure may include one or more of these actions:
   a. Remove samples from -20°C or -80°C freezer and place in styrofoam containers packed with dry ice until an alternative freezer is identified.
   b. Remove samples from -20°C or -80°C freezer and place in freezers in Translational Research Therapeutics on LL1 until the CCR freezer is functioning within designated limits.
   c. Document details of any remedial actions taken and maintain the monitoring records with CenTrak temperature log files.
   d. Remove affected participant meal trays and place in ice chest (located in file room) packed with frozen blue ice, or ice, until an alternative refrigerator that is acceptable for food storage is identified.

Continuous Cardiac Monitoring (Telemetry)

Requirements

I. All overnight rooms in the CCR are equipped for telemetry with the Phillips Continuous Cardiac Monitoring (CCM) system.
II. Education on and orientation to the CCM system will be provided during orientation to appropriate clinic personnel.
III. The CCM is inclusive of the five cardiac electrodes, the blood pressure monitoring cuff, and the Sp02 finger monitor. All three devices may be applied and utilized during CCM, enabling automatic and manual measurement of blood pressure, respiration, Sp02, and heart rate. End tidal CO2 monitoring capabilities are also available if needed for specific study requirements, such as for those with conscious sedation.
IV. Alarm parameters must be set and alarms monitored when a participant is on CCM.[4]
    a. The CCM alarm and participant call light alarms must be audible at all times while the participant is being monitored, with clinical staff available to respond to an alarm at all times.
V. Phillips CCM alarms are monitored on an on-going basis by CCR personnel. All clinic personnel will assist the clinic RN when a participant is on active monitoring by notifying the RN immediately if an alarm sounds.
VI. Only RNs may assess, interpret, and/or make changes to the plan of care based on alarms. An ECG complex diagram is shown in Appendix A for reference.
VII. A provider must be available (on call) to address any concerns about the patient's status while on CCM, and the correct contact telephone number must be included in the clinical order for monitoring.

Procedure

I. The CCR RN will provide education to the participant and family members, if applicable, on the following aspects of CCM:
    a. Reason(s) for monitoring
    b. Need to remain on the unit and connected to the monitor at all times, unless ordered by physician
    c. Need to report symptoms such as chest pain, dizziness, or shortness of breath by alerting the nurse via the participant call system
    d. Potential risks of disconnecting monitoring equipment
II. The CCR RN will connect the participant to the monitoring system and perform ongoing monitoring.

[4] Sound the Alarm: Managing Physiologic Monitoring Systems, Joint Commission Perspectives on Patient Safety. Association for the Advancement of Medical Instrumentation (AAMI) Alarms Systems National Patient Safety Goal on Alarm Management: The Joint Commission. December 2011;6-8, 11.

a. The CCR RN will confirm that the CCM is current with Clinical Technology inspection prior to using the equipment.
b. Place the cardiac monitoring electrodes correctly and verify the cardiac waveform.
c. Connect the blood pressure cuff and Sp02 sensor, placing them correctly on the participant, as described in "Vital Signs".
d. Set alarm parameters and alarm volume.
e. Monitor and respond to alarms promptly.
f. Adjust alarm parameters as clinically indicated.
g. Communicate and collaborate with other members of the health care team regarding alarms.
    i. Before taking the participant off-monitor (e.g., for showering, toileting, or upon discharge), the RN will confirm that requirements for being off monitor (as determined by the study provider/MD or study protocol) are met.
h. Assess the participant and family needs for on-going education about CCM.
i. Document the procedure and associated activities in the participant's study record.

Controlled Substances: Distribution and Control

Requirements

I. Use and handling of controlled substances is subject to both state and federal regulations. CCR personnel and clinical research groups utilizing CCR services must comply with proper licensing requirements by the states and the US Department of Justice Drug Enforcement Administration (DEA) record keeping, inventory, and handling requirements at 21 CFR Chapter II.
II. All individuals and organizations who handle controlled substances must be registered with the DEA. A unique number is assigned to each legitimate handler of controlled drugs and this number must be submitted to the supplier prior to the purchase of controlled substances.
    a. Nurses who administer controlled substances within their scope of practice are not required to have a DEA number.
    b. Registered individuals and organizations are required to:
        i. Maintain accurate inventories and records of all controlled substances transactions
        ii. Securely store controlled substances
        iii. Maintain controlled substances records separately from other records
        iv. Follow procedures for administering, documenting, storing and controlling access to controlled substances

Responsibilities

Medical Director

The medical director will hold the DEA license for the CCR and will be responsible for keeping the DEA-222 forms in a secure, locked location. The medical director supervises the assistant clinical director.

Assistant Clinical Director

The assistant clinical director is responsible for implementing and maintaining controlled substances policy in the CCR, and for providing and documenting follow-up actions for any discrepancies reported. The assistant clinical director authorizes Pyxis access and privileges for any licensed nursing staff.

- The assistant clinical director will establish the Pyxis security levels and authorize access for each employee and will ensure that deactivation occurs for employees separated or placed on investigatory leave.
- The assistant clinical director may give permanent Pyxis access to career, per diem, traveler, and registry staff.
- Any inappropriate use of Pyxis access or codes will result in disciplinary action, up to and including termination.

Nurse

All authorized nurses will accurately document the administration and disposition of controlled substances to participants in the Pyxis electronic record in compliance with unit procedures.

All personnel

All personnel are required to follow CCR procedures. Failure to comply with the controlled substances procedures will result in disciplinary action, up to and including termination.

Procedure

I. Ordering drugs
   a. The physician ordering a controlled substance will use the Form 222 special order form issued by DEA that includes the preprinted name and address of the registrant for every instance of Schedule 1 or 2 controlled substances orders.
   b. The order form is completed in triplicate with one copy maintained by the CCR, and two copies (copies 1 and 2) going to the supplier, who keeps one and forwards the other to the DEA after filling the order. The physician may appoint a licensed designee (such as the clinic director) to order the controlled substance but will be the signer on the 222 form.

II. Receiving and Stocking
   a. The supplier staff member delivering the medications and a CCR licensed personnel (nurse, pharmacist, physician) will perform an inventory and reconciliation of medications delivered.
   b. The CCR licensed personnel[5] will confirm the inventory as correct and sign for receipt of the medications, documenting on the purchaser's copy (copy 3 of DEA 222) the actual number of packages received and the date received.
   c. Two licensed CCR personnel (nurse, pharmacist, physician) will load the received medications into Pyxis.

III. Storage and Record-Keeping

[5] The requestor and receiver must not be the same individual.

a. Two licensed staff members will conduct a weekly inventory of controlled substances medications stored in the CCR Pyxis; inventory is documented electronically in Pyxis.

IV. Administration and Waste
   a. The physician must write an order for every medication administered in the CCR.
   b. The nurse must administer medication according to the "5 Rights" of medication administration:
      1. Right patient
      2. Right medication
      3. Right dose
      4. Right route
      5. Right time
   c. CCR personnel will add the participant's name and medical record number to the Pyxis profile.
   d. The nurse will remove medication from Pyxis for a specific participant.
   e. The nurse will document administration[6] of controlled substances medications to participants in the participant's CCR chart, noting the response to the medication administered.
   f. The nurse will accurately document any waste of controlled substances in Pyxis, with confirmation by a second licensed CCR personnel.

V. Audits
   a. CCR authorized personnel will perform random audits at least biennially or as needed.
   b. Any authorized individual may conduct an audit at any time.

VI. Discrepancies
   a. The nurse must notify the assistant clinical director immediately if a controlled substances discrepancy is noted.
   b. If a discrepancy cannot be resolved, the assistant clinical director or designee will investigate and document relevant findings in a written report, describing the incident, the date/time, and the names of the individuals who identified the discrepancy.
   c. The assistant clinical director or designee will notify the medical director and other relevant authorities, as appropriate.

VII. Notification of Authorities
   a. The medical director or designee will notify the DEA using an electronic report form DEA Form 106 if there is unresolved discrepancy or loss, or reported or suspected theft of controlled substances.
      1. If loss, theft, or diversion is suspected or confirmed, the medical director or designee will notify the appropriate authorities, which may include, but not be limited to:

[6] Controlled substances are used for participants within the CCR only. No controlled substances are dispensed for outpatient use.

a. California State Board of Pharmacy
b. Relevant licensing board (Board of Registered Nursing, Medical Board)
c. University of California Police Department (Thornton/Cardiovascular Center
d. San Diego Police (Hillcrest),
e. California State Department of Justice
f. UC San Diego Health Regulatory Affairs

2. The medical director or designee will report thefts, diversion, and/or significant discrepancies that cannot be explained or recovered to UC San Diego Health chief executive officer and other senior leaders.

Electrocardiogram (ECG/EKG) – 12 lead

Electrocardiogram is a non-invasive procedure used to ascertain information about the heart's electrophysiology. Consistency and accuracy are important in obtaining standard 12-lead ECG tracings. The PI or designee is responsible for ensuring that a 12-lead ECG required by the study protocol is ordered and also for ensuring that any sponsor-specific protocol requirements, such as use of a specific machine and/or serial measurements, are met. The PI or designee is also responsible to analyze and interpret the ECG tracing, and to arrange appropriate follow-up for all abnormalities.

Personnel Competency

Only personnel who are appropriately trained and practicing within their scope of practice may perform ECG procedures.

Procedure

I. Gather required equipment and supplies, including, but not limited to:
   a. 12-lead ECG machine,[7] utilizing study-specific equipment as required by study protocol and provided by PI
   b. ECG electrodes
   c. Alcohol swabs
   d. Adhesive remover swabs or washcloth
   e. 2X2 gauze pads
   f. Razor (if needed)

II. Verify the study participant's identity (name and date of birth), verifying that the identifiers match the research record.

II. Confirm study-specific requirements for acquisition of serial tracings or multiple ECG copies.

III. Confirm the identifiers or study codes required in the ECG machine and on the tracing against the orders, protocol, and/or by querying the PI, designee, or study coordinator.

[7] CCR equipment GE MAC 3500 (user manual)

IV. Explain the ECG procedures and answer any questions, as appropriate, that the study participant may have about the ECG procedure. Refer questions from the study participant to the investigator or study coordinator if needed.
V. Ask the study participant to remove clothing from the waist up and don a hospital gown with the opening to the front, ensuring privacy by closing the curtain and/or the exam room door.
VI. Enter the relevant identifiers and required collection data into the ECG machine.
VII. Prepare the skin for electrode placement by cleaning with alcohol swabs, shaving, as required, then drying the prepared areas with gauze pads.
VIII. Place the electrodes and attach lead wires using the diagram[8] from the ECG cable as a reference.
IX. Acquire the ECG tracing(s).
X. Confirm the tracing is adequate. Troubleshoot any interference or missing lead data and repeat acquisition as needed.
XI. In the event that the study sponsor provides a specific ECG machine for study use, the CCR clinical staff will acquire the tracing using the sponsor-provided equipment. The investigator's designee will save, store, and transmit the data as required per protocol.
XII. Remove the lead wires and ECG electrodes; clean the skin with adhesive swabs or a warm, moist wash cloth.
XIII. Print the required number of ECG copies.
XIV. Provide ECG copies to the PI or study coordinator; place one copy in the study participant's CCR chart.
XV. Document the procedure in the participant's study record.

Emergency Procedures

Medical emergencies are unexpected events that lead to bodily injuries or medical conditions/crises. The types of medical emergencies that can occur in public places, including health care facilities, are numerous and varied, but some examples include:

I. Loss of, or altered, consciousness
II. Respiratory distress/respiratory arrest
III. Myocardial infarction (MI)
IV. Sudden cardiac arrest
V. Hypoglycemia
VI. Asthma attacks
VII. Allergic reactions (see Anaphylaxis)

Procedure

I. Notify the PI or designee if study participant experiences any alarming, unexpected and/or potentially serious event, including, but not limited to:
    a. Change in level of consciousness

[8] Aimcardio.com – 12 lead placement guide

b. Sudden onset of confusion or agitation
c. Difficulty breathing
d. Chest pain
e. Allergic reaction to study medication

II. For study participants with diabetes mellitus who experience change in level of consciousness or sudden onset of confusion or agitation, check finger stick glucose.
   a. If hypoglycemic:
      1. If CONSCIOUS, ABLE TO SWALLOW, AND ABLE TO TAKE ORALLY, give fast-acting carbohydrate, choosing ONE of the following according to the "Hypoglycemia Protocol Outpatient Study Orders":
         i. 1 tube glucose gel OR
         ii. 4 glucose tablets (16 grams) OR
         iii. 4 ounces juice OR
         iv. 8 ounces skim milk
         a. Following administration of fast-acting carbohydrate, repeat fingerstick glucose in 5 minutes.
         b. If no change in glucose level, repeat the fast-acting carbohydrate dose as above and notify physician.
      2. If UNCONSCIOUS OR UNABLE TO SWALLOW:
         a. Initiate IV and activate EMS by calling 911.
   b. If hyperglycemic, activate EMS by calling 911.

III. If a study participant becomes unresponsive, implement emergency procedures as follows:
   a. Summon help by activating nurse call system and remain with study participant.
   b. Activate EMS by using **RED** telephone at nurse's station, which connects directly to EMS, or if using unit telephone, dial 3-6111.
      1. Be prepared to provide information (3W's):
         a. **Where** – Physical Address: **9452 Medical Center Drive, La Jolla, First floor suite 1E402**
         c. **What** – briefly describe what occurred
         d. **When** – notify dispatcher when incident occurred and current status
      2. Obtain automated external defibrillator (AED) at nurses' station.
      3. Attach AED as soon as available. If rhythm is amenable to shock, defibrillate and then immediately start cardiopulmonary resuscitation (CPR).
      4. Check pulse for ≤ 10 seconds. If no pulse, initiate high quality CPR following current CPR standard protocols.
      5. Every 2 minutes, check pulse, check rhythm, and switch compressors, as high-quality CPR and changing rescuers every 2 minutes improves victim's chance of survival.
      6. Be prepared to provide report of incident and interventions to first responders/EMS.
      7. Document incident, treatment and personnel present in the research record.
      8. Notify CCR assistant clinical director, who will, in turn, notify the CCR medical director.

9. Complete iReport.
10. Following transport of study participant by EMS, conduct incident review with clinical personnel and on-site clinical leadership.

Extended Stay

Requirements

I. The outpatient CCR is not approved for stays longer than 23 hours and 59 minutes.
II. Participants who require clinical care that exceeds 23 hours and 59 minutes must have their visits conducted in an in-patient research unit.
III. Participants who require longer care intervals can be discharged, reassessed by a provider, and be readmitted to the CCR, provided specified criteria are met.
IV. All overnight studies, with the exception of sleep studies, will require 2 clinical personnel, including 1 RN and either an LVN or technical personnel.
    a. Extended stay visits will be charged for RN rate regardless of whether RN is required for study protocol.
II. The study PI or designee will be available by phone at all times while the participant is in the clinic.
III. Exceptions for complex extended stay visits may be made and approved by the assistant clinical director and/or medical director depending on clinic resources.
IV. Participants who meet the following criteria are eligible for multiple consecutive day stays in the outpatient CCR:
    a. The required study procedures do not carry anticipated high risks requiring ongoing inpatient monitoring.
    b. CCR anaphylaxis procedures are adequate for anticipated adverse reactions to investigational product administration.
    c. The study participant is stable and does not have any active symptoms of chronic or acute disease processes such as shortness of breath, chest pain, or fever.
        1. If the participant requires special services such as assistance to the bathroom, a caregiver, or meals, the study team is responsible for notifying the CCR personnel at least 48 hours in advance.
        2. If the participant is at risk of fall or is cognitively impaired/confused, the study team is responsible for arranging assistance staff.
        3. Participants will meet discharge criteria within 23 hours and 59 minutes.

Procedure

I. Observational Trial
    a. Observational studies are a type of study that has no diagnostic, preventative, or therapeutic intervention applied to affect participant outcomes.
    b. Participants will require assessment by a physician **before** 24 hours of stay have elapsed.

c. Documentation of "eligibility for discharge" must be appropriately noted in the participant's records each day.

II. Interventional Trial

a. Interventional trials are defined as a research study that tests the effects of a diagnostic, preventative, or therapeutic intervention on health-related outcomes in research participants.

b. Prior to the participant leaving the clinic, the investigator or a licensed designee must evaluate the participant to determine that the participant meets discharge criteria and order the discharge.

c. Extension of stay beyond 23 hours must be appropriately documented in the participant's record.

d. Participants who require extended stays must be evaluated by the investigator or a licensed designee to determine that the participant meets discharge criteria and order the discharge.

e. The discharge must be recorded prior to hour 24 of the participant's stay.

f. Following discharge, the participant may be readmitted to the unit on a consecutive day.

g. If the participant does not meet discharge criteria before 24 hours, the PI will be notified and make a determination about whether to transfer the participant by ambulance to the emergency department. An iReport will be submitted. The study team will be notified in the event that a serious adverse event report[9] is required.

Fall Prevention

Requirements

I. Identify and intervene with study participants who are at risk for falls in order to provide a safe environment.

II. Participants who meet one or more of the following criteria are considered at risk for falls:

a. Fall within previous 6 months
b. Use of cane, walker, or crutches
c. Confused, comatose, or sedated
d. Low blood pressure
e. Needs assistance with walking
f. Difficulty getting out of a chair
g. Dizzy, lightheaded, or unsteady gait

Procedure

I. If participant meets fall risk criteria, implement one or more of the following interventions:

[9] 21CFR312.32(a)

a. Ensure call light is within reach
b. Orient participant and family member to surroundings, white board, call bell
c. Assist to bathroom if necessary
d. Place yellow sign on door
e. Educate on calling for assistance, if needed
f. Room close to nurses' station if possible
g. Provide slip proof shoes or slippers
h. Ensure brakes are locked on gurneys and exam tables
i. If participant has 3 or more fall risks, study team must ensure caregiver or staff are with the participant during the visit.

Intravenous Therapy

Requirements:

I. Identify practice standards for peripheral intravenous catheter (PIV) insertion, maintenance, and care; intravenous (IV) therapy administration.
   a. Peripheral venous access devices comprise of short PIV catheters.
   b. At the ACTRI CCR PIV catheters are placed for investigational product infusion or PK blood draws as ordered by the primary investigator.
   c. The PIV site is selected to accommodate the patient's vascular access needs based on the prescribed therapy or treatment regimen, length of treatment, duration of dwell time, vascular integrity, and patient preference.

II. Short PIV catheters may be placed by:
   a. Registered Nurses (RNs) with completion of department or unit-based orientation requirements.
   b. Licensed Vocational Nurses (LVN) with a state IV certification.

III. A provider order is required for insertion and discontinuation of PIV catheters.

IV. Pre-insertion procedure for short PIV catheters:
   a. Perform hand hygiene
   b. Provide patient with explanation and indication for the PIV insertion.

V. Insertion procedure for short PIV catheters: For insertion procedure refer to: Lippincott® Solutions, IV catheter insertion.
   a. Use approved pre-packaged IV insertion kit
   b. Preferred IV gauge of 22 or 20 depending on participant vascular condition
   c. Clean selected site with CHG or 70% isopropyl alcohol (allow to dry)
      1. Site selection should be in upper extremities unless provider order indicates another site.

VI. Discontinuation and Re-site for Short PIV Catheters:
   a. A. For the removal procedure, refer to Lippincott: IV catheter removal. Upon removal, notify provider if catheter is not intact.

b. When the PIV catheter is no longer appropriate for the prescribed therapy.

Measurements: Anthropometric Measurements, Height and Weight

Requirements:

I. Reliable and reproducible measurements require accurate, calibrated equipment.[10]

a. Height measurements for adults require a fixed stadiometer with a vertical backboard and moveable headboard.
   1. Standing height is the distance from the soles of the feet, without shoes, to the top of the head while the study participant is standing erect and looking straight ahead.
   2. Height measurements will be obtained after study participant has removed hair ornaments, ponytails, braids, etc. that may reasonably interfere with accuracy of measurement.
   3. Height measurement will be recorded in centimeters (to nearest tenth).
   4. The personnel obtaining height measurement will read the stadiometer with eyes on the same level as the headboard.

b. Weight is measured with a calibrated, electronic digital scale or beam balance.
   1. Study participant will void prior to weight measurements, and will remove shoes to be weighed in street clothes; wedding rings and eyeglasses are permitted. If required by protocol, study participants will remove any other articles of clothing or jewelry.
   2. For subsequent weight measurements, study participants should wear the same or similar clothing.
   3. If a metabolic weight is required, weigh the gown separately, then obtain the weight of the gowned study participant. To derive the study participant's metabolic weight, subtract the weight of the gown from the weight displayed on the scale.
   4. Weight measurement will be recorded in pounds or kilograms, as required by protocol.

c. Anthropometric measurements
   1. Anthropometric measurements require accurate skinfold calipers, and non-stretchable tape measure.
   2. Anthropometric measurements required by protocol will be obtained in accordance with the protocol instructions.

[10] Casadei K, Kiel J. Anthropometric Measurement. StatPearls.

3. If the protocol does not specify methodology for obtaining anthropometric measurements, standardized published methods[11,12,13] will be followed.

Procedure – Height

I. Verify the study participant's identity (name and date of birth), verifying that the identifiers match the research record.
II. Explain the procedure to the study participant.
III. Ask the study participant to stand on the floor against the stadiometer with the feet flat on the floor, heels of both feet together, toes pointed slightly outward, body weight evenly distributed, and arms hanging free at the sides with palms facing the thighs.
IV. Confirm that the heels, buttocks, shoulder blades, and back of the head are in contact with the vertical stadiometer and the body is aligned and positioned vertically above the waist.
    a. Some study participants may not be able to achieve full contact of heels, buttocks, scapulae and back of head against the vertical stadiometer board and if so, ensure the study participant is positioned so that the heels and buttocks are in contact with the vertical board and the body is aligned and positioned vertically above the waist.
IV. Align the study participant's head in the Frankfort horizontal plane as in Appendix B Height, with the horizontal line from the ear canal to the lower border of the orbit of the eye being parallel to the floor and perpendicular to the vertical backboard. This means the head is not tipped forward or backward, but rather the study participant is looking straight ahead.
V. Instruct the study participant to look straight ahead, take a deep breath, and stand as tall as possible, holding that position while the examiner brings the horizontal headboard firmly to the top of the head with sufficient pressure to compress the hair.
VI. Record the measurement to the nearest 0.1 cm.
VII. Repeat for a total of three measurements and record the average measurement, if any variation in measurements is recorded, in the study records.

Procedure - Weight

I. Verify the study participant's identity (name and date of birth), verifying that the identifiers match the research record.
II. Explain the procedure to the study participant.
III. Place the electronic scale in the kilogram (kg) or pound (lb) mode as specified by protocol-required weight units by pressing the LB/KG key on the scale keyboard face.
IV. Zero the scale by pressing the "zero" key on the scale keyboard face so that the digital LED readout shows 000.00.

[11] Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report. Instructions for Measuring Waist Circumference, According to NHANES III Protocol.
[12] Lohman T, Roche AF, Martoll R. Anthropometric Standardization Reference Manual, 1988.
[13] Obesity Education Initiative. Assessment and Classification of Overweight and Obesity. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report. Pages 56-61.

V. Ask the study participant to step on the scale and stand still, with weight evenly distributed on both feet, in the middle of the platform with head erect and eyes looking straight forward.
VI. Read and record the weight accurately to the nearest 0.1 kg/lb.

Metabolic Study Guidelines: Research Diets

The Registered Dietitian/Nutritionist (RDN) is responsible for the management of research diets in metabolic protocols.

Procedure

I. Study participants in metabolic balance studies will be informed as part of the consent process of special dietary requirements and restrictions prior to study diet initiation.
   a. Weight stability is necessary throughout the study period to support protocol requirements.
   b. Weight gain or weight loss during the study period introduces unknown variables that may affect the final study results.
   c. Study participants must be served and eat their meals in their room. That is, study participants are not permitted to visit with other study participants during mealtimes.
   d. Study participants in metabolic balance studies may not eat outside food; only foods provided by the Research Registered Dietitian Nutrition may be consumed.
II. Metabolic diets will be prepared and delivered to research participants according to the study protocol.
   a. Research diets will be customized to meet exact specifications for energy needs and macro-/micro-nutrient composition, as per the research protocol.
      1. Special dietary requests from the study participant will be reviewed and approved by the RDN and study coordinator/PI, if allowed by the research protocol.
   b. Research diets will be provided on meal trays that have been precisely weighed on Mettler electronic balance scales to the 0.10 gram weight, to assure that menu items meet study participants' individual calorie requirements.
   c. Individual activity level and/or stress factors will be included in the calculation of daily caloric requirements.
   d. Meal rounds will be conducted by the RDN to assess study participants' dietary compliance and tolerance.
      1. Leftover foods are carefully weighed and charted in the study record.
   e. Usual meal times:
      1. Breakfast: 0800
      2. Lunch: 1200
      3. Dinner: 1700
         a. Exceptions to the above meal times are permitted if:
            i. Fasting labs are required
            ii. Protocol study medication and/or tests determine meal times

iii. Study participants are off the unit on pass

4. Metabolic balance meals are to be served by the assigned research nurse or study coordinator, and the time of consumption recorded in the medical chart and source document as applicable.

Pediatric Research Participants[14]

Requirements

I. Pediatric research participants are considered to be a vulnerable population and require additional regulatory protections.
II. Pediatric research participants ≥ 2 months of age may be seen in the CCR.
III. The PI, assistant clinical director, clinic manager, clinic personnel and all associated personnel work together to ensure that pediatric research participants, including their parents and/or legal guardians, are treated in a safe, ethical, and compliant manner.
IV. All clinic staff providing direct clinical care will undergo pediatric ambulatory care training.
V. All clinic RNs will maintain current pediatric advanced life support (PALS) certification.
VI. Parents/legal guardians may stay with the child during the study visit.
VII. Older children (e.g., adolescents) may request that the parent/guardian not be present for a portion of the study visit. In the event there is disagreement between the parent and the adolescent, the PI will address the situation with the family and the CCR nurse will document the outcome. The CCR nurse will notify clinic leadership of the event.

Procedure

I. A copy of the parent/guardian permission form and the child assent, if applicable, will be maintained in the CCR research record.
II. CCR personnel will assess and weigh all pediatric research participants upon admission, using age-appropriate equipment available in the CCR.
III. CCR personnel will maintain current pediatric anaphylaxis kit[15] on-site.
IV. CCR personnel caring for a pediatric research participant who is receiving an injectable investigational drug will ensure that the pediatric anaphylaxis kit is at the bedside for drug administration.

Procedural Sedation

Procedural sedation, formerly called “conscious sedation” is a drug-induced depression of consciousness to facilitate a procedure during which study participants respond purposefully to verbal commands, either

[14] Rose CD. Ethical Conduct of Research in Children: Pediatricians and Their IRB (Part 2 of 2). Pediatrics. 2017 Jun; 139(6):e20163650. doi: 10.1542/peds.2016-3650.
[15] List of required contents of adult and pediatric anaphylaxis kits with medication and supplies’ expiration dates are maintained by clinic leadership for reference.

alone or accompanied by light tactile stimulation. Reflex withdrawal from a painful stimulus is not considered a purposeful response. With procedural sedation, no interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained; procedural sedation has a minimal effect on cardiovascular function.

Requirements for Procedural Sedation

I. Facilities
   a. Procedural sedation requires the following equipment and conditions:
      1. Adequate lighting to monitor the patient, and a source of back-up lighting in case of power failure
      2. Sufficient space for all personnel, monitoring equipment (to include cardiac monitor, pulse oximeter, BP monitor, EtCO2 monitor), and emergency equipment
      3. Adequate power outlets and clearly labeled outlets connected to the hospital emergency power supply
      4. Reliable means of two-way communication to summon help
      5. Ability to provide immediate changes in study participant position, including the Trendelenburg position
      6. Resuscitation equipment, appropriate for age and size of participant, to include:
         a. AED in close proximity
         b. Ambu bag
         c. Oxygen
         d. Airway adjuncts
         e. Suction equipment
         f. Sedation reversal agents, including Romazicon (flumazenil) and Narcan (naloxone).
         g. Source of oxygen adequate to provide study participant with at least 10 liters per minute flow of oxygen for a minimum of one hour along with devices needed for the appropriate delivery of the oxygen (i.e., regulators, nasal cannula, pulse oximetry, and face mask for O2 administration needs greater than 6L) and a full back-up source (i.e. E-type cylinder) with regulator
         h. Functional self-inflating bag and mask system for adults and pediatric study participants or flow-inflating bag with oxygen source and appropriate size mask for a neonate, if applicable
         i. Functional system to perform oral/pharyngeal suction
         j. Functional cardiac monitoring equipment

II. Continuous Monitoring

a. A physician, nurse practitioner (NP), physician assistant (PA) or RN who is credentialed and competent in procedural sedation will continually monitor the study participant.
b. Throughout the procedure and recovery period, the following parameters will be monitored and documents:
    1. Cardiac monitoring (ECG)
        a. Every 5 minutes intra-procedure
        b. Every 15 minutes post-procedure; every 5 minutes X 3 if additional sedative/analgesic or reversal medication is administered.
    2. Pulse oximetry
        a. Every 5 minutes intra-procedure
        b. Every 15 minutes post-procedure; every 5 minutes X 3 if additional sedative/analgesic or reversal medication is administered.
    3. Respiratory Rate
        a. Every 5 minutes intra-procedure
        b. Every 15 minutes post-procedure; every 5 minutes X 3 if additional sedative/analgesic or reversal medication is administered.
    4. Blood pressure
        a. Every 5 minutes intra-procedure
        b. Every 15 minutes post-procedure; every 5 minutes X 3 if additional sedative/analgesic or reversal medication is administered.
    5. Level of consciousness
        a. Every 5 minutes

III. Personnel Competency

a. Only CCR RNs, NPs and/or PAs who have documented training and competency validation in procedural sedation procedures may be permitted to administer procedural sedation under the direction of a physician who is present and is also privileged to perform procedural sedation. To train and document competency for non-physician licensed providers for procedural sedation:
    1. Provider must be RN, NP, or PA
    2. Provider must complete the live procedural sedation course and test (i.e., adult) within 6 months of hire
    3. In adult care areas, provider must complete an American Heart Association accredited advanced cardiac life support (ACLS) course or the UC San Diego Advanced Resuscitation Training (ART) course which provides ACLS equivalent education.
    4. To maintain and validate ongoing competency, the provider must successfully complete the procedural sedation test every two years.
    5. Documentation of training and competency will be captured and maintained in the learning management system electronic records.
b. Attending physicians:

1. Must have medical staff attending membership status.
2. Must be granted the privilege to perform procedural sedation via the credentialing process as follows:
    a. Apply for the privilege per the Departmental Delineation of Privileges form via the credentialing process of the Medical Staff
    b. Completion of the live procedural sedation course and the test
    c. In adult care areas completion of an American Heart Association accredited ACLS course or completion of the UCSD ART course which provides ACLS equivalent education
    d. Approval by the Credential Committee and the Medical Staff Executive Committee (MSEC)
    e. Physicians n Anesthesiology, Emergency Medicine, Trauma Critical Care, Pulmonary Critical Care, Neurocritical Care and Neonatal Intensive Care are privileged for procedural and deep sedation
    f. Re-credentialing is required by successful completion of the procedural sedation test every 2 years

c. Fellows and senior residents:
    1. Must be enrolled as a trainee in a fellowship program or a post-graduate year (PGY) 3 or above resident in residency training program with an active California Medical License
    2. Must acquire the competency to perform procedural sedation per UCSDH Policy 370.1 (Sedations for Procedures). The trainee's training program director and the Medical Staff Executive Committee must endorse the individual trainee as competent in procedural sedation and identify the acquired competency on the Intranet UCSDH "Resident Procedure Competencies" for trainees
    3. Residents in Anesthesiology and Emergency Medicine, as well as fellows in Trauma Critical Care, Pulmonary Critical Care, Neonatal Intensive Care and Neurocritical Care are exempt from this while administering sedation under direct supervision of an attending physician in the respective specialties
    4. For fellows and senior residents to acquire procedural sedation credentials, they must:
        a. Be a PGY 3 or above resident in a residency program, or in a fellowship training program with an active California medical license
        b. Complete the live procedural sedation course and the test. EXCEPTION: If previously established competency documented by Department/Division Chair or Training Program Director, this requirement can be substituted with completion of the procedural sedation online module and the test

c. Complete an American Heart Association accredited ACLS course or the UC San Diego Health ART course which provides ACLS equivalent education
d. Be approved by the Training Program Director and the Medical Staff Executive Committee
e. Be identified on the UC San Diego Health Intranet "Resident Procedure credentials" for trainees.
f. Be proctored as follows:
    i. The first three procedures will be proctored by an attending physician privileged in procedural sedation.
    ii. Feedback of these proctored cases to the Training Program Director is required.
    iii. The attending of record for the procedure requiring procedural sedation will be a physician privileged in procedural sedation.
g. Be supervised. Trainees not credentialed to perform procedural sedation must do so under direct attending supervision. The supervising attending must be present in the procedural area for the entire duration of the operation/procedure, and must be credentialed to perform procedural sedation themselves.

Procedure

I. Pre-Procedure
    A. Document study participant identification using two forms of identification and documented consent.
    B. Document history and physical assessment:
        1. History and physical assessment documentation are required for any procedure requiring procedural sedation, anesthesia, or post-procedure observation of the study participant elsewhere in the hospital. (Refer to Medical Staff Rules and Regulations for details on history and physical requirements).
        2. A same-day, pre-procedure assessment of the study participant's medical status must be documented by a physician signing the pre-procedure assessment.
        3. Immediately preceding sedation for procedures, the procedural sedation credentialed RN will obtain and document vital signs.
        4. The procedural sedation credentialed RN will discuss any abnormalities of the study participant's observed vital signs and/or physical condition with the physician.
    C. Perform procedure time out with the entire team in the location where the procedure will be performed:
        1. Verbalize and verify as correct:
            a. Study participant identification (name, date of birth, medical record number)
            b. Procedure

c. Location of procedure
d. Study name/IRB number

2. Document the time out in nursing flow sheet.

II. Intra-procedure

A. All pre-procedure documents must remain with the study participant and be part of the medical record.
B. All procedural sedation medication will be administered by the procedural sedation credentialed RN.
C. A physician's order for all medications and doses given during the procedure will be documented in the physician orders and signed by the physician prescribing the medications. The signed administration form will serve as the physician order for medication and treatment received; a separate physician order sheet is not required, unless the visit is recorded in EPIC, in which case a written order in EPIC is required.
D. Verbal orders: For any verbal orders from the physician to the procedural sedation credentialed RN, the RN will complete a verbal order read back prior to administration and document this in the medical record.
E. Documentation of medications administered will include medication drug name, dose, route, administering personnel, and time given.
    1. Medication administration:
        a. Medications used for procedural sedation should be drugs easily titrated for procedural sedation purposes, including, but not limited to, midazolam and fentanyl. Medications with specific pharmacologic reversal agents are strongly preferred. This include benzodiazepines (flumazenil reversal) and opiates (naloxone reversal). The reversal agents flumazenil and naloxone must be readily available wherever procedural sedation is administered.

III. Post-procedure

A. All pre-procedure and intra-procedure documents will remain with the study participant as part of the medical record. Records will include:
    1. Post-operative physician orders
    2. Post-procedural instructions
    3. Procedure notes
B. Post-procedural care will be conducted as per procedural sedation protocol.

IV. Recovery (Adult and Pediatric Study Participants)

A. A procedural sedation credentialed physician overseeing the study participant's care will approve discharge once discharge criteria are met.
B. Recovery criteria:

1. Recovery post-procedure with procedural sedation is determined and documented by a scoring criteria based on the discharge scoring assessment (i.e., Modified Aldrete)[16] in Appendix C:
   a. The study participant must attain a score of at least 8[17]
   b. If the total score is less than 8, or if there is a score of 0 in any category, then the study participant must be assessed for potential discharge and released by a physician overseeing the study participant's care.
   c. Other criteria related to the procedure, rather than sedation, may also be applied. These include, but are not limited to, minimal nausea and vomiting, operative/procedure site conditions (i.e., without active bleeding and/or hematoma), and/or voiding status/urinary bladder non-distended.

V. Discharge

A. Study participants may be discharged if the standard recovery criteria are met and it has been 30 minutes since the last dose of intravenous medication or ninety minutes after the last oral, transmucosal, or intramuscular drug administration.
B. If reversal agents were used, the study participant must be monitored for 90 minutes after the last reversal agent administration to ensure they do not become re-sedated.
C. Study participants who have received sedation in the outpatient setting and who are able to be discharged may not drive themselves home.
D. Study participants who have received sedation in the outpatient setting and who are able to be discharged may be permitted to take ride-share or taxi with documented PI concurrence.
E. The study participant's condition and the time of discharge will be documented in the nursing flow sheet.

VI. Adverse outcomes

A. Adverse outcomes that occur during the course of procedural sedation will be documented in the medical record. An incident report (i.e., electronic quality variance report) will be entered by CCR personnel if any of the following occur:
   1. Administration of a reversal agent
   2. Unplanned admission to the hospital
   3. Chest pain during the procedure
   4. Drop in oxygen saturation (i.e., less than 92% for greater than 5 minutes)
   5. Unintended interruption of procedure due to medication use
   6. Hypotension (Systolic blood pressure < 90)
   7. Aspiration
   8. Code blue activation (personnel initiate code blue procedures by calling 911 to have study participant transported to UC San Diego emergency department).

[16] Ding D, Ishag S. Aldrete Scoring System. StatPearls
[17] UCSDHP 370.1 Sedations for Procedures

9. Death

Privacy and confidentiality

All CCR personnel will take appropriate steps to protect research participant privacy and confidentiality. All research team members will undergo training on confidentiality and privacy protections.

Skin Biopsy

A cutaneous nerve/skin biopsy is a simple procedure performed in the outpatient setting that typically requires approximately 15 minutes. After cleaning the skin and injecting local anesthetic, a sample of skin is taken by biopsy from the anesthetized area. A sterile dressing is used to cover the biopsy site. The skin usually heals within one to two weeks; the risk of bleeding or infection is low.

Only CCR RNs with documented training and competency validation may perform the skin biopsy procedure independently. To train and document competency:

- CCR RN will observe another qualified clinician perform a skin biopsy three times.
- CCR RN will perform the procedure three times under direct supervision, with supervising clinician documenting the RN's competency
- Documentation of training and competency will be recorded in the CCR-102: Skin Biopsy Standardized Procedure Registered Nurse Competency Log.

Procedure[18]

I. Confirm the signed order for the skin biopsy is in the study participant's CCR chart.
II. Assemble the required supplies.
III. Perform a time out.
   A. Verbalize and verify correct:
      1. Study participant identification (name, date of birth, medical record number)
      2. Procedure
      3. Location of procedure
      4. Study name/IRB number

[18] Johns Hopkins Medicine Neurology and Neurosurgery Cutaneous Nerve Lab for Physicians: Cutaneous Nerve Biopsy and Analysis

B. Document the time out in nursing flow sheet.

IV. Confirm there are no known contraindication(s) to the procedure:

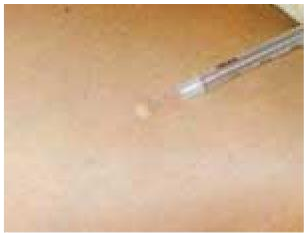
A. Individuals who are anticoagulated with International Normalized Ratio (INR) > 2.5 should not undergo the skin biopsy procedure.

B. Confirm size of skin biopsy required. Maximum size skin biopsy performed by RN is 4 mm.

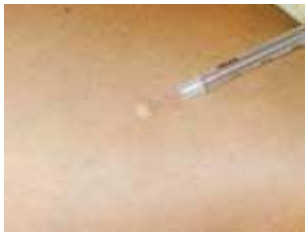
VII. Prepare the area to be biopsied.

I. Prepare the skin with alcohol swabs.

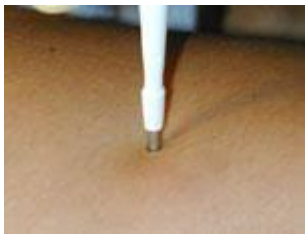
Anesthetize the skin. Once the skin has been prepared with alcohol, the next step is to anesthetize the area to be biopsied by injecting a solution of Lidocaine HCL 1% and Epinephrine 1:100,000 just under the epidermis (sub-epidermally) using a ½ cc Tuberculin syringe. The injection should continue until a "bleb" or bubble has formed under the skin greater than 3mm in diameter. The injection will burn slightly, similar to a bee string, due to a pH difference between the skin and the solution. The slight burning will quickly subside and the site will become numb (see photo below).



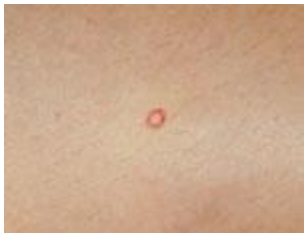
B. Check the area for numbness. After the initial Lidocaine injection, the area to be biopsied should be checked to insure that the skin is properly anesthetized. The point of the syringe is used to "poke" the area of the bleb or bubble. Care should be taken not to force the needle into the skin. The test site should be somewhere around the periphery of the bleb. Both of these precautions insure a viable biopsy for diagnosis later. If the study participant experiences neither pain nor sharp sensation, the biopsy may continue. A pressure sensation is normal and expected, but there should be no pain. If the area requires more anesthesia, another injection, using a new syringe, is made until the skin is completely anesthetized (see photo below).



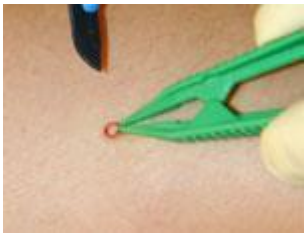
C. Biopsy the skin. After the area to be biopsied is anesthetized, the biopsy continues. Using a sterile 3 mm skin punch, the nurse applies pressure and twisting in a "drilling" motion until the blade of the skin punch has pierced the epidermis of the skin. The blade should be about ½ exposed. It is normal for the study participant to experience pressure and twisting sensation but no pain (see photo below).



D. Remove the skin punch. After the blade has sufficiently "cored" or carved out a 3 mm cylinder of skin, the skin punch is removed. It is normal for the area to bleed after the punch is removed. Excess blood is wiped away with sterile 2 X 2 gauze to expose the biopsy site. The entire process resembles the "cookie cutter" effect. The only purpose of the skin punch is to "core" the skin and not to remove the biopsy, much like a cookie cutter (see photo below).

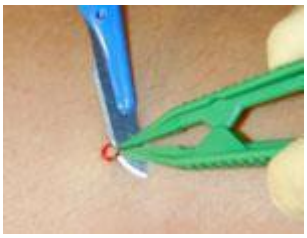


E. Excise the biopsy. When the skin has been cored and cleared of excess blood, the next step is to remove the biopsy from the rest of the skin. Great care should be taken not to damage the epidermis by crushing it with forceps or by cutting it with a scalpel unnecessarily. The operator uses the forceps to grab the dermis of the cored skin, pulls up the core to reveal excess dermis and subdermal fat, and uses the scalpel in one or two cutting motions to cut the cored skin free (see photo below).



Excise the biopsy (continued). Notice the position of the scalpel during the excision process. The scalpel is placed under the forceps and is moved in the opposite direction of the forceps pulling

on the dermis. This motion stabilizes the biopsy and aids in preventing a "chopping" or "slicing" effect when trying to free the biopsy. The operator simply utilizes one or two strokes of the scalpel to excise the biopsy with a clean cut (see photo below). Place the specimen in a properly labeled vial.



F. Bandage the biopsy site. Once the biopsy has been removed from the skin, there will usually be some degree of bleeding, which should be absorbed with sterile 2 X 2 gauze. Hemostasis should be achieved by applying direct pressure to the biopsy site. After hemostasis is achieved, gently pull skin together and place 5 steri-strips over the biopsy site. The biopsy site is then covered with folded 2 X 2 gauze and wrapped with self-adherent adhesive wrap or occlusive dressing.
G. Review biopsy site care with study participant and teach proper care.
H. Provide written instructions for home care.
I. Document the procedure in the research records.
J. Document the procedure in the Skin Biopsy Standardized Procedure Registered Nurse Competency Log, if applicable.

Standing Orders

CCR personnel may utilize standing orders when clinical circumstances necessitate prompt nursing actions while a physician is being notified. The following CCR standing orders have been developed and approved by the CCR Medical Director. The standing orders are incorporated into this manual by reference:

I. Medication Reaction/Anaphylaxis Protocol Outpatient Study Orders
II. Hypoglycemia Protocol Outpatient Study Orders
III. Sedation Reversal Protocol Outpatient Study Orders

When CCR nursing personnel execute standing orders, the investigator or designee is notified, a copy of the standing orders will be filed with the study participant's record, and all medications administered under the standing orders will be documented on the nursing flow sheet.

Topical anesthetic use

For venipuncture in children, the following topical anesthetics may be used:

I. EMLA (lidocaine/prilocaine) topical anesthetic cream may be applied ½ to 1 hour prior to scheduled venipuncture on up to 4 venipuncture sites.

Vital signs

Normal vital signs parameters:

- Oral temperature range: 97.6°F – 99.6°F
- Adult pulse range: 60-100 beats/minute
- Systolic blood pressure range: 90-140 mmHg
- Diastolic blood pressure range: 69-90 mmHg
- O^2 Saturation: 95%-100%

Alert and/or emergency referral values:

Alert values

Alert values require immediate notification of PI or designee to evaluate the study participant prior to discharge from CCR. Alert values include:

- Systolic blood pressure ≥ 180mmHg
- Diastolic blood pressure ≥110 mmHg

Document the circumstances, including the report to the provider, the provider's instructions, details conveyed to the study participant, and the study participant's condition upon discharge.

Emergency referral values

Emergency room referral is required for symptomatic study participants with alert values blood pressure, noted above, if the study participant is exhibiting symptoms, including but not limited to:

- Headache
- Chest pain
- Shortness of breath
- Visual disturbances

Document the circumstances, including the report to the provider, the provider's instructions, details conveyed to the study participant, and the study participant's condition upon discharge.

Procedure:

I. Confirm the orders and/or institutional review board (IRB)-approved protocol schedule of events procedure to be followed for obtaining vital signs.
II. Identify the study participant by confirming study participant name and date of birth and comparing stated information to information documented in study participant's CCR chart prior to performing any procedures.

III. Review ordered protocol specific requirements for obtaining the vital signs measurement with regard to study participant position, time at rest, serial measurements, temperature mode, or any other requirements.

Automated vital signs measurements using the vital signs machine

I. Oral temperature
   A. Obtain the vital signs machine.
   B. Educate the study participant on the steps in the procedure, as indicated.
   C. Connect the oral temperature probe to the machine, if not already in place.
   D. Insert the study participant contact portion of the probe into the disposable plastic probe cover and confirm a secure fit.
   E. Place the probe under the study participant's tongue in the sublingual pocket where the richest blood supply and heat are encountered.
   F. Allow the machine to record the temperature and signal the end of the measurement.
   G. Dispose of the probe/probe cover into an appropriate waste container.
   H. Record the displayed temperature in the study records.
   I. Document the procedure.

II. Blood pressure (B/P)
   A. Obtain the vital signs machine.
   B. Educate the study participant on the steps in the procedure, as indicated.
   C. Determine the appropriate B/P cuff size according to the study participant's arm circumference using the reference range.
   D. Confirm any protocol requirements for right versus left arm measurements.
   E. Position the study participant so the selected arm is at the same level as the heart.
   F. Secure the cuff around the study participant's upper arm.
   G. Confirm correct positioning of the cuff, ensuring the arterial marker on the cuff is positioned over the brachial artery with the lower edge of the cuff 2.5 cm above the bend in the elbow.
   H. Confirm the air flow lines are not pinched or kinked.
   I. Press the "start" button on the vital signs machine to initiate the reading.
   J. Once the machine signals the reading is complete, remove the cuff from the study participant's arm.
   K. Record the reading in the study records.
   L. Determine if the B/P reading requires notification to the PI or designee for evaluation and/or emergency room referral if study participant is experiencing other symptoms, including, but not limited to, headache, chest pain, shortness of breath, and/or visual disturbances.
   M. Document the procedure.

III. Heart Rate/Pulse
   A. Obtain the vital signs machine.
   B. Educate the study participant on the steps in the procedure, if indicated.

C. Complete the blood pressure measurement, as described above and record the heart rate reading from the vital signs machine console into the study records.
D. Document the procedure.

IV. Pulse Oximetry – One-time reading
A. Obtain the vital signs or pulse oximetry machine.
B. Educate the study participant on the steps in the procedure, as indicated.
C. Connect the oximetry sensor to the machine.
D. Place the finger cap sensor on the study participant's finger with the sensor's position on the side of the fingernail.
E. Record the reading in the study records.
F. Remove the sensor from the study participant's finger.
G. Document the procedure.

V. Pulse Oximetry – Continuous monitoring
A. Obtain the vital signs or pulse oximetry machine.
B. Educate the study participant on the steps in the procedure, as indicated.
C. Connect the oximetry sensor to the machine.
D. Place the finger cap sensor on the study participant's finger with the sensor's position on the side of the fingernail.
E. Secure the sensor to the study participant's finger with tape.
F. Record the readings in the study records as ordered.
G. At the end of the monitoring period, remove the sensor from the study participant's finger.
H. Document the procedure.

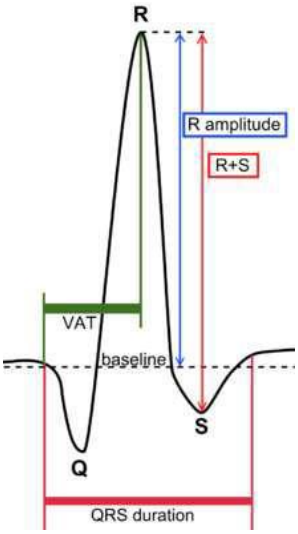
Manual vital signs measurements

I. Blood Pressure (B/P) with aneroid sphygmomanometer
A. Educate the study participant on the steps in the procedure, as indicated.
B. Determine the appropriate B/P cuff size according to the study participant's arm circumference using the reference range.
C. Confirm any protocol requirements for right versus left arm measurements.
D. Position the study participant so the selected arm is at the same level as the heart.
E. Wrap the blood pressure cuff around the study participant's upper arm, ensuring the arterial marker on the cuff is positioned correctly over the brachial artery with the lower edge of the cuff 2.5 cm above the bend in the elbow.
F. Confirm the bulb to cuff lines are not pinched or kinked.
G. Inflate the cuff rapidly to a level 30 mm Hg above palpatory systolic pressure. Obtain palpatory systolic pressure by palpating (feeling) the radial (wrist – thumb side of hand) pulse by placing index and middle finger on the radial pulse and feeling for the cessation of the pulsation while inflating the cuff.

H. Deflate the cuff at a rate of 2 mmHg per second while auscultating for the Korotkoff sounds with the stethoscope. As the pressure falls, the systolic pressure and diastolic pressure are recorded.
I. Record the readings in the study records.
J. Document the procedure.

II. Heart rate/pulse
A. Educate the study participant on the steps in the procedure, as indicated.
B. Place the index and middle finger lightly on the study participant's radial pulse (wrist-thumb side of hand) to palpate (feel) for the pulse created by the heartbeat.
C. Count the number of beats for a full 60 seconds or as required by the protocol.
D. Record the reading in the study records.
E. Document the procedure.

Appendix A – ECG Complex Diagram



Detail of the QRS complex, showing ventricular activation time (VAT) and amplitude.

A typical ECG tracing of the cardiac cycle (heartbeat) consists of a P wave, a QRS complex, a T wave, and U waved which is normally visit in 50 to 75% of ECGs. The baseline voltage of the electrocardiogram is known as the isoelectric line. Typically, the isoelectric line is measured as the portion of the tracing following the T wave and preceding the next P wave.

R-R Interval: The interval between an R wave and the next R wave. Normal resting heart rate is between 60 and 100 bpm (0.6 to 1.2s)

P wave: During normal atrial depolarization, the main electrical vector is directed from the Sino Atrial("sinus") node towards the Atrial-Ventricular (AV) node, and spreads from the right atrium to the left atrium. This turns into the P wave on the ECG (80ms).

PR interval: The PR interval is measured from the beginning of the P wave to 120 to 200ms interval to the beginning of the QRS complex. The PR interval reflects the time the electrical impulse takes to travel from the sinus node through the AV node and entering the ventricles. The PR interval is therefore a good estimate of AV node function.

PR segment: The PR segment connects the P wave and the QRS complex. This coincides with the electrical conduction from the AV node to the bundle of His to the bundle branches and then to the Purkinje Fibers. This electrical activity does not produce a contraction directly and is merely traveling down towards the ventricles and this shows up flat on the ECG. The PR interval is more clinically relevant (50 to 120ms)

QRS complex: The QRS complex reflects the rapid depolarization of the right and left ventricles. They have a large muscle mass compared to the atria and so the QRS complex usually has a much larger amplitude than the P-wave (80 to 120ms)

J-point: The point at which the QRS complex finishes and the ST segment begins. Used to measure the degree of ST elevation or depression present.

ST segment: The ST segment connects the QRS complex and the T wave. The ST segment represents the period when the ventricles are depolarized. It is isoelectric (80 to 120ms)

T wave: The T wave represents the repolarization (or recovery) of the ventricles. The interval from the beginning of the QRS complex to the apex of the T wave is referred to as the absolute refractory period. The last half of the T wave is referred to as the relative refractory period (or vulnerable period) (160ms)

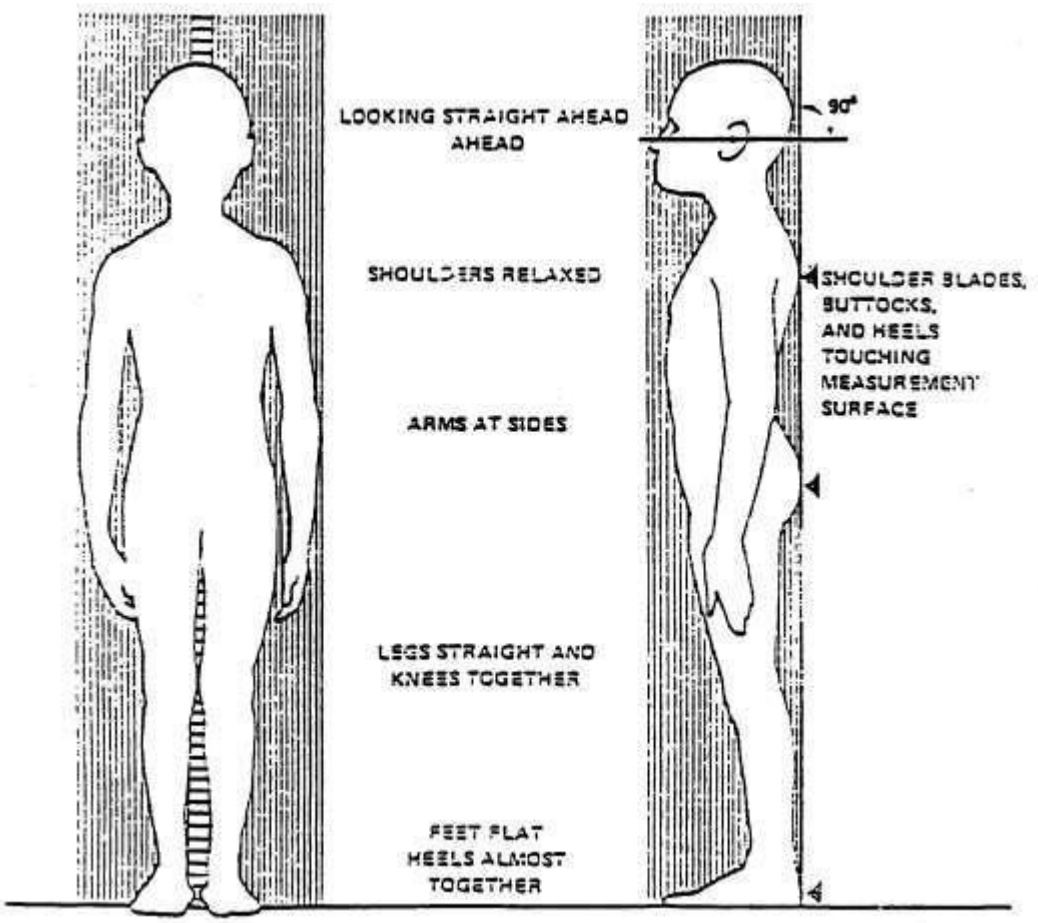
ST interval: The ST interval is measured from the J point to the end of the T wave (320ms)

QT interval: The QT interval is measured from the beginning of the QRS complex to the end of the T wave. A prolonged QT interval is a risk factor for ventricular tachyarrhythmias and sudden death. It varies with heart rate and for clinical relevance requires a correction for this, giving the QTc. (300 to 430ms)

U wave: The U wave is hypothesized to be caused by the repolarization of the interventricular septum. They normally have a low amplitude, and even more often completely absent. They always follow the T wave and also follow the same direction in amplitude. If they are too prominent we suspect hypokalemia, hypercalcemia or hyperthyroidism usually.

J wave: The J wave, elevated J-Point or Osborn Wave appears as a late delta wave following the QRS or as a small secondary R wave. It is considered pathognomonic of hypothermia or hypocalcemia.

Appendix B – Height



Appendix C – Modified Aldrete Score

Aldrete Score Table	
Activity	**Score**
Able to move 4 extremities voluntarily or on command	2
Able to move 2 extremities voluntarily or on command	1
Able to move 0 extremities voluntarily or on command	0
Respiration	
Able to breathe deeply and cough freely	2
Dyspnea or limited breathing	1
Apneic	0
Consciousness	
Fully awake	2
Arousable on calling	1
Not responding	0
Circulation	
B/P ±20% of preanesthetic level	2
B/P ±20% to 50% of preanesthetic level	1
B/P ±50% of preanesthetic level	0
Oxygenation	
Able to maintain O2 saturation >92% on room air	2
Needs supplemental O2 to maintain O2 saturation >90%	1
O2 saturation <90% even with supplemental oxygen	0