UNC
THE NORTH CAROLINA
TRANSLATIONAL & CLINICAL
SCIENCES INSTITUTE

Best Practices in Conducting Pediatric Clinical Research

North Carolina Translational and
Clinical Sciences (NC TraCS) Institute

Juanita Cuffee, MPH, CCRP, Pediatric Hematology/Oncology
Rose Cunnion, CCRC – Pediatric Pulmonology
Chayla Hart – Division of Pediatric Endocrinology

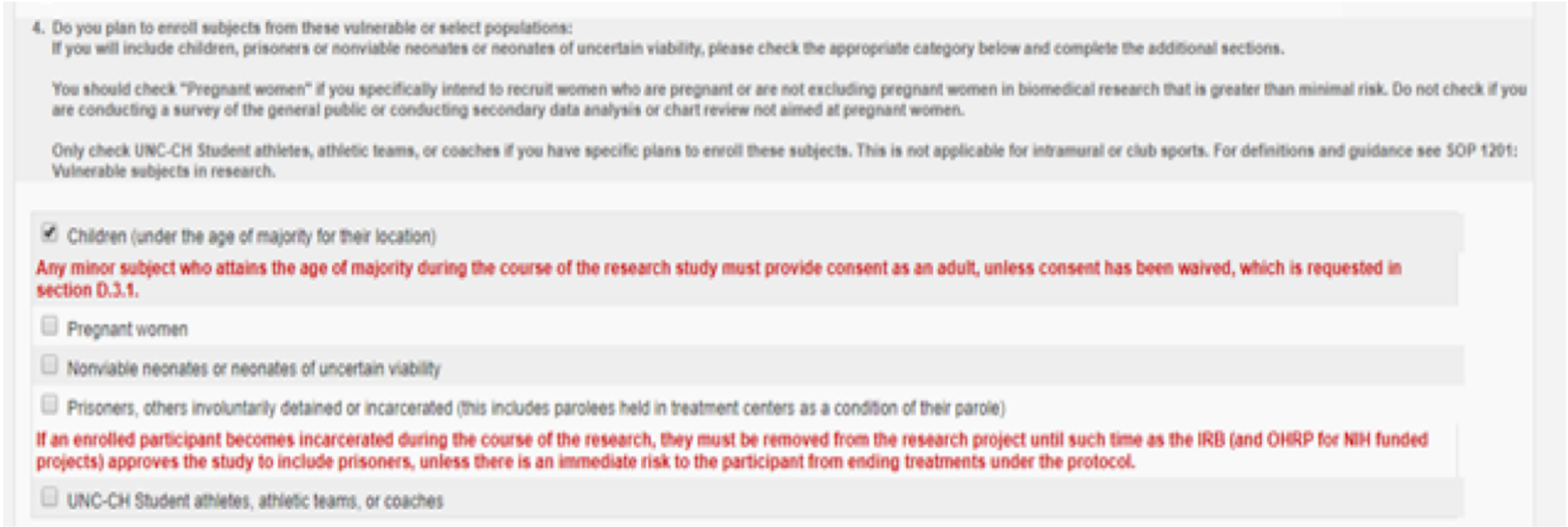
Today's Topics

- Regulatory aspects of Clinical Research with minors
- Protocol Adherence
- Safety Considerations
- Study Visits

Best Practices in Pediatric Research: Regulatory Considerations

- Clinical research in children is challenging and poses important logistical & ethical considerations that differ from adults (vulnerable population)
- Small numbers, rare diseases, limited reimbursement
- Off-labeling practices can lead to adverse safety events and efficacy concerns
- Poorly evaluated interventions adopted as standard of care later found to have lack benefit or cause harm
- Increased incentives to perform pediatric trials

IRB Application Section A.2.4



4. Do you plan to enroll subjects from these vulnerable or select populations:
If you will include children, prisoners or nonviable neonates or neonates of uncertain viability, please check the appropriate category below and complete the additional sections.

You should check "Pregnant women" if you specifically intend to recruit women who are pregnant or are not excluding pregnant women in biomedical research that is greater than minimal risk. Do not check if you are conducting a survey of the general public or conducting secondary data analysis or chart review not aimed at pregnant women.

Only check UNC-CH Student athletes, athletic teams, or coaches if you have specific plans to enroll these subjects. This is not applicable for intramural or club sports. For definitions and guidance see SOP 1201: Vulnerable subjects in research.

- [x] Children (under the age of majority for their location)

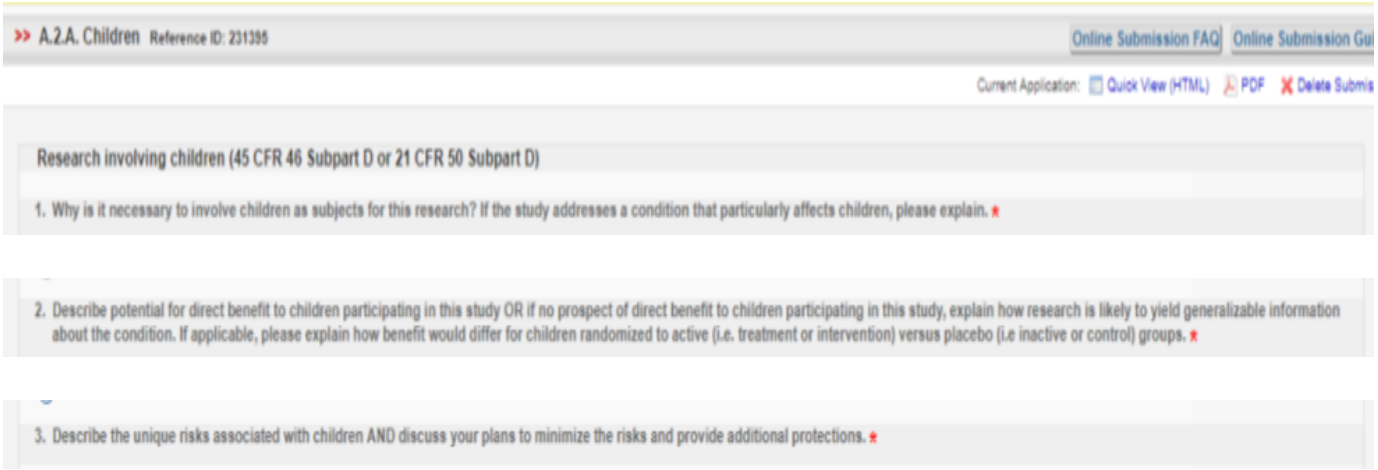
Any minor subject who attains the age of majority during the course of the research study must provide consent as an adult, unless consent has been waived, which is requested in section D.3.1.

- [ ] Pregnant women
- [ ] Nonviable neonates or neonates of uncertain viability
- [ ] Prisoners, others involuntarily detained or incarcerated (this includes parolees held in treatment centers as a condition of their parole)

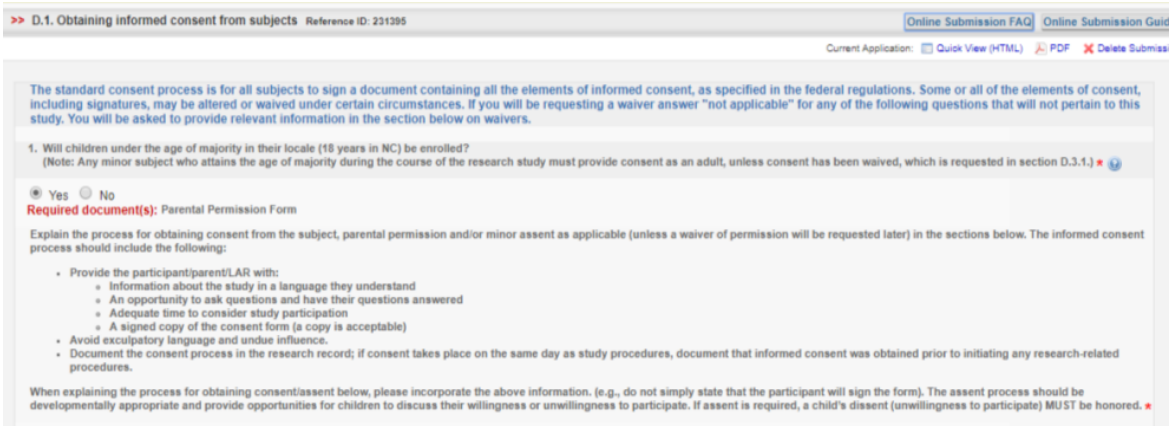
If an enrolled participant becomes incarcerated during the course of the research, they must be removed from the research project until such time as the IRB (and OHRP for NIH funded projects) approves the study to include prisoners, unless there is an immediate risk to the participant from ending treatments under the protocol.

- [ ] UNC-CH Student athletes, athletic teams, or coaches

IRB Application Section A.2.A



IRB Application Part D: Consent Process



Waiving written assent?

Writing the Informed Consent/Assent

- ICFs/IAFs/Information sheets
- Age appropriate language
- Easy terms for medical procedures
- Read sponsor template closely for unclear language
  - "If you are doing things that might get you pregnant…"
- Pregnancy testing, ages of disclosure (NC law), frequency of testing, requirement for contraception use; refer to IRB SOP 4801
- Assent template to address written, verbal, no assent
- Consider the regulations when writing the assent

Foreign Language for Consent/Study materials

- Parent requires a language other than English
- Child speaks, reads, writes fluently in English
- Translated ICFs
- Short forms
- Other study materials (diaries, questionnaires, etc)
- Translated documents by certified translators
- No hospital interpreter service; contract services - still pay if no show
- Specify on IRB Application A.2.5 & D.1.4

Special Circumstances: Legally Authorized Representative (LAR)

- Federal regulations that govern research involving human subjects define a legally authorized representative (LAR) as an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research [45 CFR 46.102(c) and 21 CFR 50.3(l)]
- Will study population necessitate a LAR?
- Legal documentation (e.g.: Court orders)
- Photo copy, place with consent, place in EPIC
- Indicate on IRB Application; update consent documents

Special Circumstances: Wards of the State

- A “Ward” or “Ward of the State” is a minor (under 18 years of age) who is under the legal custody of the State or any other agency, institution, or entity (e.g.: Case worker - DSS)
- Others terms: Legal caretaker, guardian ad litem, kinship care
- Enrolling wards of the state unexpectedly
  - IRB modification – IRB application A.2.4 & A.2.5
- HIPAA statement may need to be updated to reflect status
- Legal documents in EPIC; authorization to treat
- Foster Care/Adoption
- Involve your social worker

Documenting permission for multiple caregivers to attend/make decisions at study visits

- Parent sign consent; grandmother brings to visit, but parent makes major medical decisions
  - Ex: Great aunt has decision making authorization (notarized documents), but mom or dad is inconsistently in the picture. Who makes medical decisions?
  - Ex: Grandma or sibling bring pt to visits; can they make medical decisions? Considerations: Giving proper history, current medications, dosing, AEs
- Not a one size fits all approach for determining best practice
- Difference between consenting for SOC and consenting research procedures

Minor participant is 18, now what?

- Start gradually, prior to 18 (hopefully address shock)
- Transition study communication when a minor reaches age of majority (email address, phone number)
  - Does the young adult have a preference? Document accordingly
- myuncchart access at 18, can begin as early as 13
- Internal SOP on re-consenting and conducting study procedures in minors who attain age of majority.

Other things to consider

- Duration of document storage after study closure (standard recommendation is until the child turns 30 years of age)
  - Laws may differ by country (e.g.: Canada)
- Study compensation, who receives the money – parent or child? Concerns of coercion. Tax reporting, who's SSN to use
  - Legal guardians, foster parents

Best Practices in Pediatric Research: Protocol Adherence/Safety

Protocol Adherence

- What is your study population?
  - Condition that's being evaluated
  - Age
  - Gender

- What limitations or advantages will your population have with the protocol and study procedures?
  - Cultural considerations
  - Home-life circumstances
  - Transportation

Protocol Adherence

- Use of Investigational and Non-Investigational Products (IP) or Devices
- IP Administration other than home setting
  - Sponsor-specific recommendations
  - Disclosure of subject's participation
  - Facility Limitations (e.g., storage, personnel, etc.)
  - Local policies

Minor Participant Safety

- Awareness of unsafe situations
  - Physical signs
  - Emotional & Behavioral signs
  - Indications in conversation
  - Are caregivers in unsafe situations that place the minor(s) at risk?

- Implement a plan. You could be a first-responder!
  - Will you page your PI straight away?
  - Will you make an anonymous report to Child Protective Services together? Keep in mind the counties with which you're interfacing.
  - Do you have a Social Worker assigned to your Division?

Best Practices in Pediatric Research: Effective Study Visits

Building Rapport

- Starts with first contact with patient/caregivers – only have one chance to make a first impression!
  - Have you met them before?
  - Are you contacting them in person or over the phone?
  - Physician introduction?
- Consent process
  - Apply ICF to the patient; research their meds/background (use HIPAA waiver!)
  - Assure comprehension of child when consenting
    - Demonstrate procedures
    - Child friendly materials to introduce idea of research – "Emma Green: Science Superstar"
    - If age appropriate, explain the purpose of all tests
    - Child can say no even if parent says yes
- Be as flexible as possible with schedule
  - Nap time? Feeding time?
  - Time for breaks/play time
  - Be realistic and reduce stress!
  - Coordinate other appointments at UNC
- Some parents need control
  - Allow for this, within reason
  - Parents may need to leave the room for sensitive questions
- Communication style
  - Formal vs. informal

Building Rapport Cont.

- Identify barriers
  - Fear of needle sticks
  - Potty trained or diapers
  - Temperament
  - Boredom
  - Physical coordination
  - Cognitive understanding
- Procedural interventions
  - Distraction
  - 4% lidocaine cream
  - Buzzy Bee

- Techniques
  - Positioning
  - Focus vs. Distraction
  - Medical play
  - Choices
  - Don’t apologize

Child Life Services

- What is Child life?
  - Certified Child Life Specialists (CCLS) are trained in child development to support children in the medical environment to promote effective coping through play, preparation, education, and self-expressive activities.

- UNC Children's offers Child Life Specialists who:
  - provide non-medical preparation and support to children undergoing tests, surgeries, and other procedures
  - Help children with anxiety, pain, coping, and adjustment to hospitalization/healthcare encounters in developmentally appropriate ways
  - Help children with medication and procedure compliance
  - Foster an emotionally supportive environment
  - Consider the needs of siblings who may be affected by a child's illness or injury

Where We Started

- Heard about CF researchers at CH of Minnesota using CLS
- Set up a meeting with Pulmonary CCLS, Jordan Hullinger, to give overview of the research studies and get feedback on accessibility of CL services
  - Are you allowed to help with research?
  - Do you have time? Estimate volume of high acuity visits
  - Who needs to approve?
- Therapy Services Manager, Pediatrics: Keith Compson (keith.Compson@unchealth.unc.edu)

Start Up/Budgeting

- Amended budget and contract with Sponsor to include:
  - Hourly wages for CLS ($32.31/hr)
  - Toys/prizes
- Subject materials and incentives must be added to consent form and IRB approved

Logistics

- RC coordinates via email with Jordan when we have visits scheduled, page her when needed (sometimes a different CCLS comes dependingon availability)
- RC sends Keith the dates and time CCLS spent on each study each month
- Keith sends invoice which we bill to sponsor

Me not holding down a distressed child while parents and sibling look on helplessly!

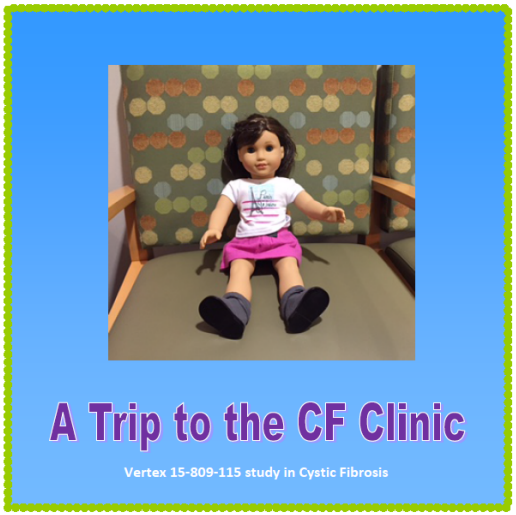
Sibling

Child Life Specialists

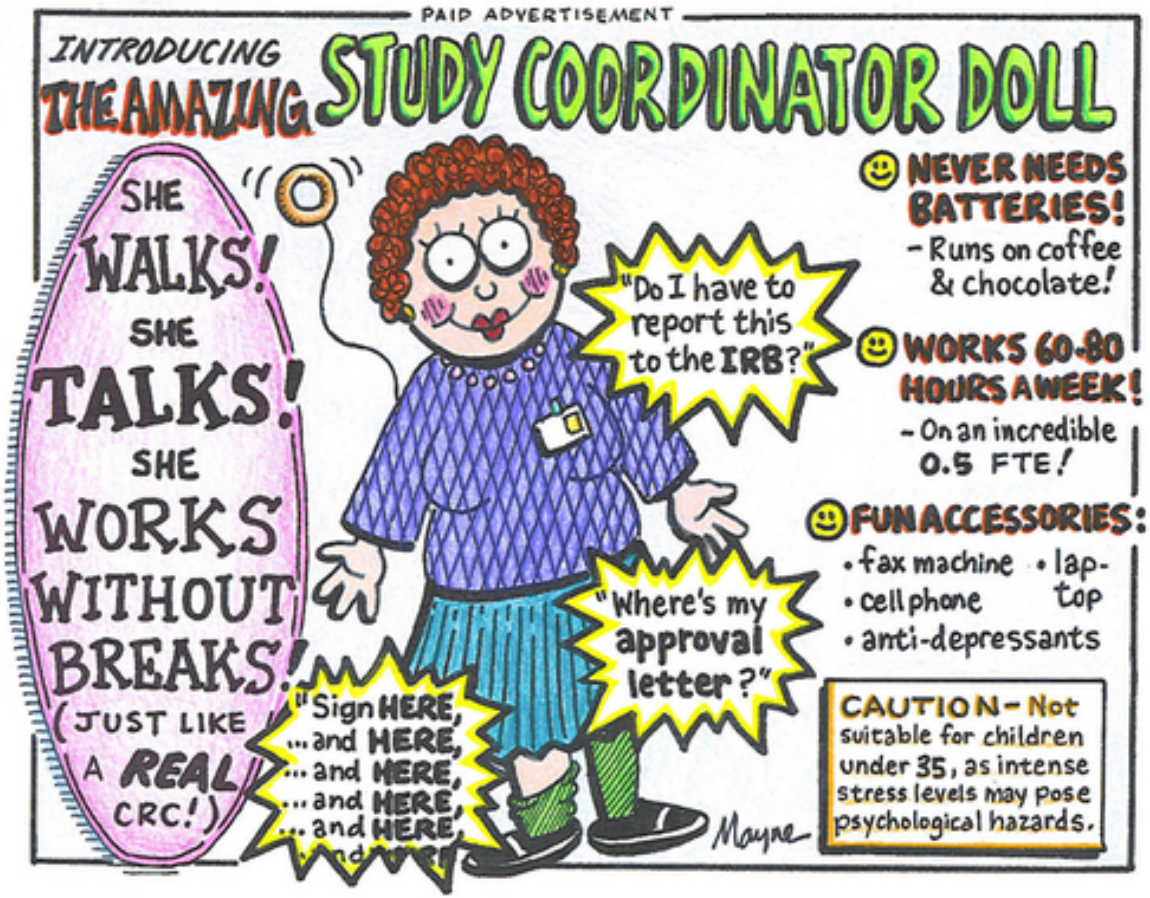
Playing

Subject undergoing sweat test procedure

- Study visit sticker book



- Study visit story board


PAID ADVERTISEMENT
INTRODUCING THE AMAZING STUDY COORDINATOR DOLL
SHE WALKS! SHE TALKS! SHE WORKS WITHOUT BREAKS! (JUST LIKE A REAL CRC!)
"Do I have to report this to the IRB?"
"Where's my approval letter?"
"Sign HERE, ...and HERE, ...and HERE, ...and HERE,
NEVER NEEDS BATTERIES! - Runs on coffee & chocolate!
WORKS 60-80 HOURS A WEEK! - On an incredible 0.5 FTE!
FUN ACCESSORIES:
• fax machine • laptop
• cell phone
• anti-depressants
CAUTION - Not suitable for children under 35, as intense stress levels may pose psychological hazards.
Mayne