Research Study Documentation
Best Practices and Common Mistakes

EQuIP
Education and Quality Improvement Program

Boston Children’s Hospital
EQuIP is
Education and Quality Improvement Program

Office of Clinical Research Compliance
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Program Purpose

To educate and update the research community of regulations regarding human subject protections

… and of good clinical practices regarding research conduct and documentation.
Program Purpose

Observe
What is going on?
See what is actually happening in practice

Educate
Communicate findings and provide materials to research community

Learn
Common strengths and weaknesses and why they occur
Observe: Study Reviews

One-time review of active study to assess current compliance and conduct:

- Random Selection
- For-cause
- PI-Requested (partial or full review)
Study Review Process

Random Selection

Initial Notification

Day of Review
1. Meeting
2. Records Review
3. Debrief

Final Report to PI

Records Identification

PI Response & Review by EQuIP

Scheduling

Closeout Notification
Study Reviews: Compliance

Is study compliant with applicable regulations, sponsor MOO, IRB-approved protocol and institutional policies?

1. Federal Regulations & Guidelines
   e.g. FDA, HHS/OHRP, NIH, OSHA

2. State and Local Laws
   e.g. Age of assent, Consent

3. Sponsor
   e.g. MOO/SOPs

4. Institutional Policies
   e.g. IRB, Policies & Procedures
**Study Reviews: Conduct**

Is study conducted in compliance with applicable regulations and policies which assure human subjects’ rights and protection and documented according to accepted standards to demonstrate the integrity of study data?

- **Best Practices** used to comply with regulations & policies

- **Good Clinical Practice (GCP)***: international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects.

- GCPs and Best Practices are **not** regulations

* Provides public assurance that the rights, safety, and wellbeing of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.
Study Reviews: Documentation

ALCOA

Attributable
- It should be clear who has documented the data.

Legible
- Readable and signatures identifiable.

Contemporaneous
- The information should be documented in the correct time frame along with the flow of events. If a clinical observation cannot be entered when made, chronology should be recorded. Acceptable amount of delay should be defined and justified.

Original
- If not original should be exact copy; the first record made by the appropriate person. The investigator should have the original source document.

Accurate
- Accurate, consistent and real representation of facts.

Study Reviews: Learn & Educate

Observe: Identify Common Errors and Unique Strengths

Educate: Develop and Implement General Education
Documentation & Organization

Ensure Complete & Accurate Documentation

- The quality of the study documentation will ultimately impact the validity and usability of the collected study data.

- Remember, it is not only important how you collect your study data, but also how you document your data.

- What study documents are required?
  - Know what is required: regulatory, sponsor and institution
  - Know where each document is filed: are documents filed in safe and secure location, that is available as needed and upon request.
  - Paper or electronic = safe and secure


**Documentation & Organization**

**Study Regulatory Binder & Subject Case Histories**

- Downloads available on [EQuIP site](#):
- Also see [Harvard CATALYST Regulatory Binder](#)

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**RESEARCH**

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**Organize Your Study**

**Organize Your Study:** Study & Subject Binders

Complete and thorough protocol documentation generally includes a Study Regulatory Binder. Documents and correspondence are stored, and individual Subject Case Histories, in which the data is maintained.

**Developing and Maintaining the Study Regulatory Binder**

The purpose of the regulatory binder is to store and organize required or useful study documents in an up-to-date and systematic manner. The binder facilitates the effective and efficient management of studies and their protocols. An organized regulatory binder may also maintain continuity in the event of staff changes or turnover.

**Study Regulatory Binders** are not required, but are considered best practice and highly recommended. The research team should be familiar with the regulatory binder, and should be designated to update the binder.

The designated person should be listed as the additional contact (e.g., the CCI) for the study to ensure that correspondence and documents are received in a timely manner. The binder should be maintained in a safe and locked location, though easily accessible to all research staff at all times.

The following documents are included in EQuIP's template regulatory binder:

- Regulatory Binder Instructions
- Table of Contents
- Contact and Resources
- Regulatory Binder

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**Subject Case Histories**

Individual subject information should be maintained separately from the regulatory binder in subject specific binders or folders. Subject case histories generally include signed informed consent forms, source documents, and completed case report forms.

**Source documents** are the hard copies on which clinical observations are first recorded. Source documentation is often the medical record, but it can also be a computer printout of lab values, patient diaries, physician progress notes, etc. **Case report forms (CRFs)** are the research instruments designed to collect the variables that are necessary to answer the research questions of a specific protocol.

The following document provides guidance on how to create, manage, and update complete individual subject case histories.

Please be sure to review the Study Visit Documentation guidance and templates, located on the Tools and Templates page for additional information and guidance on maintaining complete subject case histories.

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Documentation & Organization
Electronic Records

- Store electronic files safely and securely, for example in hospital backed-up shared drive or Sharepoint Team Site

- Avoid duplication of documents where possible (having a paper version and an electronic version)

- Follow a naming convention
Group Exercise

1. List study documents that tell you *what is required* for your specific study.

<table>
<thead>
<tr>
<th>Study Document and Requirement</th>
<th>Central Location. Filed/Stored - Paper and/or Electronic?</th>
<th>Safe &amp; Secure?</th>
<th>Available on request?</th>
<th>Responsible Person(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current IRB approved Sponsor's protocol</td>
<td>Electronic – CHERP</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>Paper – regulatory binder</td>
<td></td>
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<tr>
<td>Outlined versions of sponsor's protocol</td>
<td>Electronic – CHERP</td>
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<tr>
<td></td>
<td>Paper – regulatory binder</td>
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<tr>
<td>IRB approved recruitment flyers</td>
<td>CHERP</td>
<td></td>
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<tr>
<td>Manual of Operations (MOO) for laboratory sample collection, labeling, shipping, &amp; analysis</td>
<td>Electronic – Sharepoint</td>
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<tr>
<td></td>
<td>Paper – regulatory binder</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOP for storing and making electronic copies of signed consent forms</td>
<td>Electronic – Sharepoint</td>
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<tr>
<td></td>
<td>Paper – regulatory binder</td>
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<td></td>
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<tr>
<td>Current template and past versions of study case report forms</td>
<td>Electronic – sharepoint</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

2. List study documents that relate to *how the study was conducted.*

<table>
<thead>
<tr>
<th>Study Document and Requirement</th>
<th>Central Location. Filed/Stored - Paper and/or Electronic?</th>
<th>Safe &amp; Secure?</th>
<th>Available on request?</th>
<th>Responsible Person(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signed consent forms for all subjects enrolled to date - Three ring binder – locked cabinet/shelf</td>
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<tr>
<td></td>
<td>PDF in Electronic folder - sharepoint</td>
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<tr>
<td>Lab test results for all screened subjects</td>
<td>Individual subject case files – locked cabinet/shelf</td>
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</tr>
<tr>
<td>Completed case report forms for all screened subjects</td>
<td>Individual subject case files – locked cabinet/shelf</td>
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<tr>
<td></td>
<td>Electronic-Redcap database</td>
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</tbody>
</table>
Study Reviews: Common Errors

1. Consent Form Errors
2. Study Documentation
Conduct: Know what is required

What regulations & policies apply to your study?

1. Federal and State Regulations: HHS, FDA
2. Sponsor MOO, Institutional Policies

What are the study-specific ‘instructions’?

1. IRB approval letter
2. IRB application (in CHeRP called “smartform”)
3. Approved protocol
Conduct: Know what is required
Ensure Complete & Accurate Documentation

- Study Documents must represent what happened
  - Must be able to recreate the study as it actually happened, not as it was stated in protocol
  - Ensure study procedures (MOO/SOPs) allow for consistent documentation of any deviations from approved and accepted protocol practices
Documentation & Organization

Ensure Complete Study Documentation

- All data collection forms should be complete
  - No blanks! Missing values must be explained e.g. not obtained, n/a, missing

- Data Corrections made correctly
  - Clear audit trail
  - Never white-out, black-out or obscure corrected values. All values must be transparent.
Documentation & Organization

Simple documentation errors should be corrected in the following manner:

Subject Weight: 52 kg 110 lbs

1. Cross out mistake with one single line
2. Write the correct information next to error
3. Date and initial correction
4. If correction is not obvious, explain
Common Errors
Conduct vs Documentation

- **Documentation error**: lack of or inaccurate documentation of study activities/procedures
  - Date of birth transposed on case report form
  - Interpreter/witness involvement in consent process with non-English speaking subject not documented in writing

- **Conduct error**: not following the IRB approved protocol in the conduct of any study activities/procedures. *Conduct errors constitute protocol deviations.*
  - Posting an unapproved recruitment flyer
  - Not conducting an eligibility confirmatory lab test
  - Obtaining verbal instead of signed consent from subject
  - Miscalculating and administering incorrect study drug dose
Common Consent Errors
Conduct and Documentation

- **Documentation:**
  - Both parents participated in consent but only one parent signed
  - Minor subject lacked capacity to assent; reason no assent not documented.

- **Conduct:**
  - 2 parents permission required but not obtained
  - Minor subject capable of providing assent not consulted

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**Parent/Legal Guardian Permission (if applicable)**

*If the child to be involved in this research study is a foster child or a ward of the state please notify the researcher or their staff who is obtaining your consent.*

- Date (MM/DD/YEAR)  
  - Signature of Parent #1 or Legal Guardian
  - Relationship to child

- Date (MM/DD/YEAR)  
  - Signature of Parent #2 (if required)
  - Relationship to child

☐ CHECK if 2nd parent signature not obtained above. The PI must document in research records, the reason and/or all attempts made before concluding 2nd parent was not ‘reasonably available’.

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**Child Assent (if applicable)**

- Date (MM/DD/YEAR)  
  - Signature of Child/Adolescent Subject

- If child/adolescent’s assent is not obtained above, please indicate reason below (check one):
  - ☐ Assent is documented on a separate IRB-approved assent form
  - ☐ Child is too young
  - ☐ Other reason (e.g. sedated), please specify: ________________________________

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**Adult Subject (if applicable)**

- Date (MM/DD/YEAR)  
  - Signature of Adult Subject (18+ years)
Common Consent Errors
Conduct and Documentation

- **Documentation:**
  - Signatures on wrong line or missing
  - Dating another person’s signature
  - Misdating signature: day given, obtained or started study

- **Conduct:**
  - Outdated version of consent signed
  - Person other than legal guardian provided permission for minor subject
Common Consent Errors
Conduct and Documentation

- **Documentation**: Subject agreed to optional procedures but did not check the boxes.

- **Conduct**: Optional procedures were not discussed with subject.

Please check and initial one of the boxes below:

- I **do** consent to have my child’s DNA stored for future research.
- or -
- I **do not** consent to have my child’s DNA stored for future research.

When the stored DNA samples are studied, it is possible that we could find genetic changes that are related to
Common Consent Errors
Conduct and Documentation

- **Documentation:**
  - Involvement of interpreter/witness not documented on consent form or elsewhere in record of consent process
  - Non-English speaker parent / subject did not sign / date short form consent

- **Conduct:**
  - Subject and family given copy of signed short form but not signed English language consent document
  - Short form method of consent followed for a greater than minimal risk study for which IRB approval to use short form method not granted

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Short Form Consent to Participate in Research

Boston Children’s Hospital

MRN:
DOB:
Subject’s Name:

Short Form Consent to Participate in Research

You are being asked if you want to join a research study. Before you agree to join the study, a member of the study team must tell you some things about the research. You will be told:

a. the purpose of the research
b. what will happen to you during the research
c. how long the research will take and how long you will be asked to participate
d. any parts of the research that are experimental (something that is being tested)
e. any risks or parts of the research that might hurt you or make you feel uncomfortable
f. any benefits to you or others that could come from the research
g. any treatments or procedures that might benefit you instead of the research (alternatives)
h. some identification of whom your data will be shared with
i. about how your confidentiality and the privacy of your information will be protected

The study staff must also tell you the information below if it applies to this study:

a. if you will receive any compensation (money or free medical treatment) if you are injured while you are in this research study
b. if there might be risks that we don’t know about now but could happen in the future
c. if there are reasons why the researchers may stop you from being in the study
d. any costs for you for being in the study
e. what happens if you want to stop being in the study
f. when you will be told about new findings that may cause you to change your mind about being in the study
g. how many people will be in the study.

After you are told all the information above the study staff will ask you if you want to be in the study. If you agree then the study staff will ask you to sign this form. You must be given a signed copy of this form in your own language. You will also be given a written summary of the research in English.

You or your interpreter may call _________ _________ at _________ _________ any time you have questions about the research or what to do if you are injured. You or your interpreter may call the Children’s Hospital Committee on Clinical Investigation at 617-355-7022 if you have questions about your rights as a research subject.

You are free to decide whether or not you want to be in this research study. It is up to you. You can decide that you do not want to be in the study. You can decide to be in the study and stop at any time. If you decide not to be in the study or if you decide to stop you will not lose any benefits to which you are entitled. No matter what your decision it will not change the way you are treated by the staff but if you decide to be in the research study it could change your treatment plan.

Signing this document means that the research study was explained to you. This means that you were told all of the information above. If you sign this form it means that you agree to be in the study.

Printed name of subject: __________________________ Signature: __________ Date: __________

Name of person obtaining consent: __________________________
Signature: __________________________ Date: __________

Printed name of witness: __________________________ Signature: __________ Date: __________

* Witness ensures that research protocol was described and the subject was advised they could ask questions
Welcome to the Children's Hospital Research Informed Consent Library (IC Library)

This library contains currently approved protocol informed consent documents. Consents for protocols that have been terminated will not be included. Investigators/Research coordinators should use the ICLibrary website each time they need a copy of the consent form to distribute to a participant. Do not store consent forms on your computer. One of the main benefits of this database is to ensure that the latest copy of the consent is always used.

Please use the textboxes below to search the IC Library. You may enter any combination of Protocol #, Protocol Title, PI Last Name and PI First Name. Press the "View Report" button to display the results. If you need help, please call CHeRP Support at extension 4-3267 or email CHeRP.Support@childrens.harvard.edu.
Consent /Assent Best Practices

- Know what is required for your study
- Review the consent immediately, in real-time
- Use Informed Consent Library (via CHERP)
- Train staff obtaining consent & update as needed
- Document the consent process somewhere other than the actual consent/assent form (e.g. study visit note)
Tracking and Reporting Protocol Deviations to the IRB
Sample Deviation Log

Children's Hospital Boston

Protocol Deviation Log v.2

Principal Investigator

Protocol Title

Protocol #

CH/CCI policy requires Principal Investigators (PIs) to report all protocol changes, deviations and exceptions to the Committee on Clinical Investigation (CCI). Upon discovery, if the PI deems the event a significant deviation (affects subject safety, risks or benefits, data integrity and/or subject's willingness to participate), a Significant Deviation Form must be completed and submitted to the CCI within 72 hours.

Otherwise, all other minor deviations should be documented, filed with study records, and a copy submitted to the CCI with each continuing review application. The following form is a template that may be used to document minor deviations for study purposes, and/or to submit to the CCI with the next continuing review. This form is not required by the CCI.

<table>
<thead>
<tr>
<th>#</th>
<th>Description of Deviation</th>
<th>Date of Deviation</th>
<th>PI: Significant or Minor?</th>
<th>PI Signature and Date</th>
</tr>
</thead>
<tbody>
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<td>* notify CCI within 72 hours</td>
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<td></td>
<td>□ Significant</td>
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<td>* notify CCI within 72 hours</td>
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<td>* notify CCI within 72 hours</td>
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<td></td>
<td></td>
<td>* notify CCI within 72 hours</td>
<td></td>
</tr>
</tbody>
</table>
Continuing Renewal Form
Tracking & Reporting Deviations to the IRB

Note: In accordance with current federal regulations, the Institutional Review Board (IRB) must review the risk/benefit ratio for protocols at least annually. To avoid any lapses in approval, please complete this form. If approval lapses, no research related activities may occur after the expiration date unless the investigator contacts the IRB office and the Chair determines that it is in the best interests of an individual subject to continue during the lapse of IRB approval. If protocol is complete, please submit a completion report, not a continuing review.

### Protocol Status

1. Select the appropriate category to indicate the current status of the protocol.
   - Currently enrolling subjects
   - Closed to new enrollment: Treatment and/or research assessment/interventions continue
   - Closed to new enrollment: All research activities complete, long term follow-up only
   - Closed to new enrollment: All research activities complete, data analysis only
   - No subjects enrolled to date
   - Other

   **If Other:**
   1.1 Please explain.

### Deviations and Exceptions

2. Select all categories that apply (more than one may be checked).
   - No prior protocol deviations or exceptions have occurred since the original approval.
   - Prior deviations/exceptions occurred on this protocol, and already acknowledged or approved by the IRB.
   - Unreported minor deviations or exceptions that have occurred since the last review, and significant deviations not yet reported, are attached for review.

2.1 Please upload the minor deviations/exceptions for review.

<table>
<thead>
<tr>
<th>Name</th>
<th>Date Last Modified</th>
<th>Version Owner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exception Log.doc</td>
<td>6/20/2012 12:06 PM</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Note: If a significant deviation needs to be reported, please open a reportable event.

### Protocol Reliance

3. Has another institution relied on Children’s Hospital IRB to eliminate duplicative review?
   - Yes
   - No

   **If YES:**
Study Tools, Templates and Guidance

RESEARCH

Study Tools and Templates

Some of the tools and templates on this site may not be the most recent version. Contact the EBUIP Office at 657-620-8208 if you have questions about whether a newer version is available.

The study tools and templates provided are intended to help researchers:

1. Document required information
2. Organize study documents
3. Track study procedures

First, take the time to think about what data is required; and then select a template to build from. Do not use a template unless all data you will collect, but rather modify the template to collect the data you need. Since you have a template selected, customize the form to fit the specific needs of the study and research team. When tailoring the template, remember to:

- Use a legible font and font size
- Provide ample space to enter complete and legible data
- Only collect data that is required and useful for the study and staff (remove fields if they will not be used)
- Design the form to be user-friendly -- easy to update, understand and maintain
- Consider where the form will be filed and how it will be updated (electronically or paper) - must be safe and secure, but accessible for updating and reference.

To use any of our study templates below, click on the template name to open the document in MS Word format. For more detailed description and ideas on how to use the template, click on the corresponding Guidance document (if available).

Pre-Study Set-Up
Research Staff and Training
Study Organization Tools
Study Tracking and Documentation Tools

Pre-Study Set-Up: Checklists
Education: Guidance and Resources

- Educational Presentations
  - Study Team/Groups
  - Department/Division

- Educational Initiatives and Materials
  - CCI/IRB Newsletter “Memo-to-File”
Memo-to-File: from the EQUIP Office

The following are a few Best Practices identified during recent EQUIP Studies:

Use the Informed Consent Library to access current consent documents:

One of the most common deviations noted during study reviews is when superseded, or un stamped consent documents. The most effective way to avoid this deviation is to use the CHERP Informed Consent Library to access the most current, stamped consent forms. Every time the research team prepares to consent a new study team members are trained to verify the correct consent version and stamp.

Track and Report Minor Protocol Deviations according to CCIRB policy:

Protocol deviations are considered unintentional events that depart from the study protocol and are identified retrospectively. Per CCI/IRB Policy, Investigators should promptly report all deviations within 72 hours of awareness and assess whether minor or significant. Significant deviations are tracked and will depend on the type of research and the study; minor deviations are documented, and reported in aggregate at the time of continuous review. Sample Deviation Log is provided on the EQUIP website, and can also be used to create individual Memos to File, or include a description of the deviation abstracted from the larger study activity database to meet this requirement.

Follow the Study-Specific, IRB-approved Recruitment and Consent/Assent Process:

There are many recruitment methods and materials a research team may use to contact subjects, such as mailings or scripted phone calls to eligible patients/family members, phone calls, e-mails, and placing advertisements in specific media. However, recruitment materials must be selected as appropriate for each study and IRB-approved prior to use. Unlike the amendments to the protocol, the informed consent/assent can vary (e.g., in-person, phone and/or mail, amended consent form, etc.) and must be IRB-approved prior to use. Make sure everyone on your study team understands the recruitment methods and materials for both recruitment and consent processes by verifying the IRB-approved protocol and corresponding CHERP smartform sections.

Memo-to-File: from the EQUIP Office

Consent is not a document signed and dated before a subject is enrolled in a study; rather it is an on-going process documented throughout a subject’s participation in a study.

The following are a few Best Practices identified during recent EQUIP Study Reviews:

- **Identifying the need for re-consenting**

  When the IRB approves an amendment that involves new information which may affect the subject’s willingness to continue participation in a study, the investigator is required to inform the subject/family before the next study visit/procedure as part of the on-going consent process. Like any other study procedure, the research team should document this in the subject’s study record (e.g., Memo-to-file, study visit checklist). Depending on the type of research and information, the IRB may require that active subjects are re-consent with the amended consent form prior to further study participation.

- **Identifying and promptly consenting subjects who turn 18 while still enrolled in ongoing research**

  Unless the requirement has been explicitly waived by the IRB, any minor subject enrolled via parental permission and assent that subsequently turns 18 while enrolled in a research study must be consented as an adult prior to continued study participation. Research where this typically occurs would be that involving longitudinal follow up, prospective review of medical records, or ongoing sharing of samples via a repository. Research teams should develop and implement a method to track and identify in real-time minor subjects who turn 18 during a study. E.g. add a field which calculates age to an enrollment log or database and alerts research team when a subject turns 18 in relation to subsequent study visits/follow-up contacts. See related CCIRB Guidance.

Visit the EQUIP website for more information and resource or call Eunice Newbert or Susie Corl at the EQUIP...
Questions?

- Eunice Yim Newbert  5-5308
  Eunice.newbert@childrens.harvard.edu

- Susie Corl  5-5308
  Susan.corl@childrens.harvard.edu