June 2016

Human Subjects Protection Update

IRB (Institutional Review Board) *Boston Children's Hospital*

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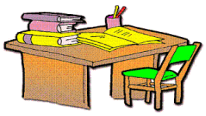
A Message from the Director



This spring has been very busy in the IRB office. In March we underwent our third **reaccreditation site visit**. The site visit was three days, and over 50 individuals were interviewed. This included investigators, coordinators, IRB members, IRB staff, a member of the pharmacy, the radiation safety officer and others that support the human research protection program at BCH. The accreditation agency had many positive things to say about our program and had only two small and correctable findings, which is the least we have ever had. The findings involve 1) the timing for IRB review of conflicts of interest including any associated management plans and 2) the criteria that IRB members use to determine whether a protocol needs to be deferred. These findings and associated corrective actions are important for investigators to understand since it may impact the time required for review and approval of a protocol. We received full accreditation in June after we corrected these findings. Please review the articles in the newsletter that further describe the findings and subsequent changes made.

The accreditation visit was immediately followed in by an unannounced **inspection of the IRB by the Food and Drug Administration** in April. There were no findings after 2 days of inspection.

In addition, I want to call to your attention that we have carefully evaluated the **timing and operational flow** of new protocols, amendments, and continuing reviews in the office. Every submission is important to review in a timely manner. All submissions are reviewed by the IRB analysts in the office for completeness before being sent on to the IRB members for review. IRB analysts need to prioritize what is submitted on an ongoing basis. A pre-review of a new protocol both needs to be completed and responded to by the research team before it is put on an IRB agenda. After an IRB meeting investigators are anxious to receive their reports of action. Many amendments may seem very simple and straight forward and could be reviewed quickly; however amendments cannot always take priority as it will impact the timing of review of other types of protocol submissions. If you are noticing that amendments may take a little longer to approve than in the past, it is because we are continually prioritizing all submissions. Last year we had over 4,000 amendments submitted. During the past year we have implemented the ability for investigators to process their own BCH staff changes in CHeRP, so it no longer requires IRB review. This will significantly reduce the number of amendments we receive (see newsletter article as a reminder of this process). We are committed to processing all submissions in a timely manner and are continuing to monitor our metrics. You should feel free to contact our office as necessary if there are critical timing issues and we will do what we can to accommodate you.

Lastly I want to inform you that there are some indications that a change to the **federal regulations governing human subject protection** may be published in September. Some of the proposed changes may impact consent for the use of biological specimens. There are potentially many other changes as well. As you may remember when the proposed changes were published for comment, there was controversy and opposition to many of the proposed changes, however it is still possible these or modified changes will go forward. I will continue to keep the community updated if I receive any additional information. Enjoy the summer and as always please contact our office as you need assistance.

Thank you,

Susan Kornetsky

Reports of Action: Conditional Approval versus Deferral

When the IRB reviews a protocol they often have, comments, questions and required revisions. The federal regulations govern what types of questions and responses need to be reconsidered by the full IRB. During our last accreditation site visit it was noted that there were many conditional approvals which should have been deferrals and as such the responses needed to go back to the full IRB for review. We are all aware that it takes additional time to put responses back before the full IRB; however this finding needs to be corrected. The following are the criteria that the IRB must use for designating a review as a conditional approval. The report of action must contain questions or issues limited to:

1. **Confirming** specific assumptions or understandings on the IRB regarding how the research will be conducted.

2. **Providing direct, clearly stated stipulations and parameters** with which the investigator can agree.

3. **Requesting additional documentation** (e.g., certificate of ethics training) not related to the regulatory criteria of approval .

4**. Providing precise language changes** to protocol or informed consent documents.

All other types of questions or concerns need to come back to the full IRB for review. The IRB would like to avoid deferrals as much as the investigators, as it increases their workload as well. In an effort to try and avoid excessive number of deferrals please note the following steps the IRB will begin taking:

1. The IRB reports of action will be much more directive instead of open ended responses. You do not need to agree to the changes that are requested and may respond accordingly. The IRB is not trying to dictate how you perform your research but rather making some assumptions and requirements may help move the protocol forward more quickly. If the IRB does not have enough information or the protocol presents significant ethical or regulatory considerations, they will still need to defer the protocol and review the responses at a convened meeting.

2. You may receive correspondence during the weekend or Monday morning before the IRB meeting asking you to address some questions prior to the meeting. We have asked IRB members to communicate issues that may signal a potential deferral during their review to the administrative office so we can try and get additional information to bring to the meeting. The IRB office will contact you through CHeRP, using the "Contact Research team" message, so please respond as quickly as possible. We begin our meetings at 11:30 AM on Mondays and the IRB members usually review the protocols over the weekend. This means we will be contacting you with short notice to respond before the meeting. Also note these preliminary questions are likely to be from the assigned primary and secondary reviewers and responding to them does not guarantee an approval or conditional approval. The full IRB will still need to discuss the protocol at the meeting. Other issues or comments from other members may be raised during the IRB meeting. It is also possible that if there are too many detailed issues or concerns you may not be contacted prior to the meeting.

3. You may be contacted by phone during the IRB meeting when your protocol is being discussed. We will try to contact you beforehand, if we think there is a possibility we will need to call in order to determine your availability. We cannot contact everyone as this may depend on the number of protocols we have to discuss at any given meeting, timing constraints, and the nature of the protocol concerns.

Even with these extra steps, it is possible the number of deferrals will increase. We ask investigators to do their part by submitting detailed protocols that address human subject concerns. Also please carefully respond to the pre-review comments by the IRB analysts as they have in-depth knowledge of the IRB considerations. The IRB members often comment that they see the IRB administrator asked the question or required the change during pre-review, but the PI choose not to address the issues. We also realize that coordinators often provide responses; however it is essential that the PI, who is a subject matter expert, review these responses before submission to make sure the response contains enough detail.

Conflict of Interest Review by the IRB

The IRB (or IRB member assigned an expedited review) is required to approve any conflict of interest (COI) management plan as it pertains to human subject protections. This may be as simple as agreeing that a consent form should disclose an investigator's previous consulting work with a company sponsoring a clinical trial or it may be a more complex management plan. All conflicts disclosed in the IRB application are initially reviewed by a conflict of interest officer who is part of the Compliance Office at BCH. The compliance office will provide recommendations or advise the IRB on any management plan that has been recommended; however the IRB or expedited reviewer must review the final recommendations and accept it or require additional protections.

In the past we have allowed the COI review and IRB review to occur simultaneously. Given the findings during our reaccreditation process, this now needs to be corrected so that the IRB or expedited reviewer has access to the final recommendations of the Compliance Office. This means that for any protocol that includes a disclosure, the IRB administrative office will wait until the review and recommendations by the COI officer is made and entered in CHeRP. Research teams do not need to do anything differently at this time. However we will hold and coordinate the review so that the IRB has the information it needs. This may add some additional time to process your protocol. It is important to note that the majority of protocols submitted have no disclosures, so this will not have an impact. The Compliance Office and COI officer are aware of the time constraints and the need to process these disclosures in a timely manner. If you have questions about a disclosure you are making and would like some advice prior to the protocol submission you may call the Compliance Office for assistance at any time (857) 218-4681 (internal x84681).

IMPORTANT REMINDER about Consent Form Bar Codes: BCH IRB Policy Requires Storing Most Consent Forms in the Medical Record

In 2012, in collaboration with the Medical Records department, the IRB Office devised a means to allow signed research consent forms to be easily included into the appropriate section of a research subject/patient's medical record. Research consent forms include headers with a barcode for studies where consent forms should be included in the subject's medical records. *This is the current process but we are also exploring other options for the future with medical records that may make the process easier.* The consent template includes this header. Our recent audits of investigator's indicate in many situations, the consent is not being scanned into the medical record.

Important note: You must print out a new consent form for each subject in order for the bar codes to be read by the scanner. Photocopies of consents with a bar code will produce images that cannot be easily scanned and the consent will not be placed in Power-Chart. This is the current process but we are also exploring other options for the future with medical records that may make the process easier.

To remind investigators and study teams about this procedure and how it affects their studies, we have put together this FAQ.

Q1: Why are you doing this?

A: Children's policy and good research ethics dictate that, particularly for studies that implicate present or contemplated clinical care, or that produce clinically relevant and reliable results, it is important that a subject's participation in the research, as well as certain results, be reflected in the medical record. In addition there may be safety reasons why it is important for other health care providers to know that a subject is a participant in a research study. There are some limited situations when the fact that a subject is a participant research should not be disclosed in the medical record; however these situations are usually the exception not the rule.

The template for research consents is developed to be transparent about who at BCH may know that a subject is participating in research. Therefore, the inclusion of the consent form in the medical record will become the more common approach at the hospital.

Q2: What protocols need to have their consent forms placed in the medical record and have the associated bar codes on their consent forms?

A: It is important to note that with a change to electronic medical records and electronic scheduling and ordering systems, it is difficult to keep the fact that a subject is in research confidential and only known by the research team. For example you may need to schedule a visit as a research visit or order a test to be billed to a research fund. This now creates a record of research participation in the electronic records of the hospital.

All active consent forms need to include headers but only those which need to be included in the medical record will include the bar code. When the IRB office finalizes an informed consent they will include either the bar code or a notation "Do not place in medical record." The IRB will make a protocol-by-protocol determination, but generally the following criteria apply.

For research undertaken at Children's Hospital for the intervention, treatment, or diagnosis of a disease, disorder, or condition (e.g., drug and device trials; comparison of psychological interventions; testing new diagnostic techniques), the consent form should be placed into the patient's medical record.

** In general for research where the hospital clinical electronic systems are used to schedule visits, order tests or analyze results the consent should be included in the medical record. However, for research that does not involve procedures, interventions, treatments that are part of a subject's care, diagnosis, or treatment, and the hospital electronic systems are not used; the investigator may consider storing the informed consent document and associated research data in his or her research files only. Examples of such research include: studies that involve genetic screening or testing where a diagnosis has not been confirmed; or psychiatric/behavioral assessments not intended for clinical use; and completion of questionnaires on sensitive issues that have not already been documented in the medical record.

Q3: Does the requirement apply also to Assent Forms and Short Forms?

A: Yes. If the informed consent for parental permission includes the bar code any associated assent forms and short forms also need to be included into PowerChart. The assent form and short form templates have also been updated with new headers and barcodes.

Q4: What if my protocol has a consent form for subjects who are not patients and there is no medical record. Where should their consent forms be stored?

A: If the study does not fit the criteria for requiring a consent form being stored in the medical record, then their consent forms should be stored in your own research records. Note however that performing some research procedures, such as performing an MRI on subjects who are not patients of the hospital will cause a BCH medical record to be created for your subjects even if they are not current "patients" at BCH. In such cases it is important to remember this and to inform the subject that they will have a medical record created. Please see guidance on imaging studies that are performed for research for further information: http://www.childrenshospital.org/~/media/research-and-innovation/office-of-clinical-investigation/119-special-confidentiality-issues--research-imaging102815.ashx?la=en.

Q5: How do I send my consent forms to be scanned into PowerChart?

A: All research consents that need to be sent from the following campuses should be in an interoffice envelope labeled Medical Records Boston. Drop off locations at the satellites/campuses are as follows:
** Lexington: 2nd floor Pediatric clinic
** Peabody: Front registration desks on the first floor or second floor
** Waltham: Front desk in the 2 East work room

If you have any questions regarding drop off locations, please ask the department administrators in the location in question. Most clinical areas have a drop-off location for Medical Records. Persons on the main campus can deliver their consent forms to Health Information Services (Medical Records) in the Fegan sub-basement. In the event that Medical Records cannot scan your documents for any reason they will need to have a contact name and number. Please make sure that the research consents are sent with a post-it note attached that indicates where the documents are from and a call-back number where Medical Records can reach you in case they have questions for you about the documents.

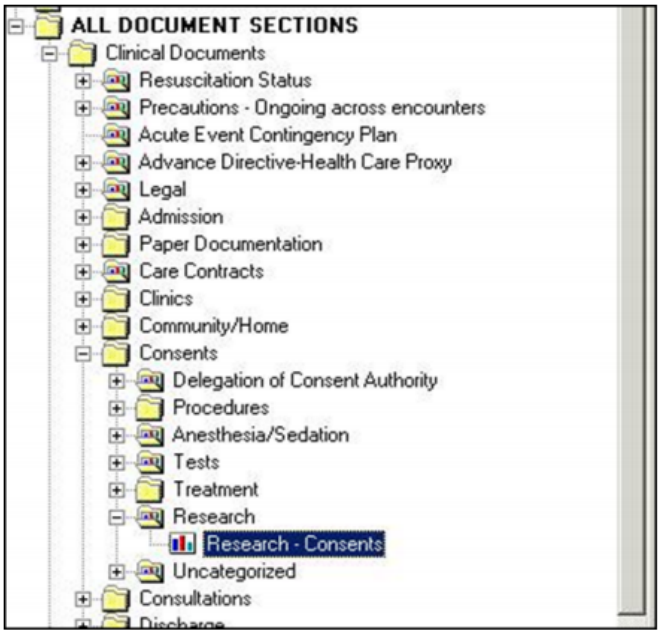
Medical Records. Alternately you can use a barcode label affixed to the header of a photocopy.

Q6: Can I send a photocopy of the signed consent form ?

A: No. You cannot send a photocopy of the consent. You must only send a copy that has been printed. . A photocopy of the barcode—even a good one—will not work. Each consent form that you send for scanning into PowerChart must be an original first-generation print-out of the consent form and not a photocopy. You must print a fresh one for each subject that you enroll and make sure that the signed original is used for scanning. In cases where you need to retain the original signed consent form for your own study records, you should make a photocopy of the signed consent form and print a fresh first page with the barcode on it and use the copy with fresh first page for sending to Medical Records. Alternately you can use a barcode label affixed to the header of a photocopy.

Q7: Once it gets scanned, where will a research consent form be placed in the medical record?

A: The consent form will be stored in Clinical Documents\Consents\Research section of PowerChart (see below).



Q8: What happens to the paper copy of the consent after it is scanned into the medical record?

A. Consent forms sent to medical records cannot be retrieved once they are sent for scanning. Investigators are advised to retain copies of all consent documents that they send to Medical Records.

Involved in Multi-Site Research? Consider an IRB Reliance Agreement!

As a leader in pediatric research, Boston Children's Hospital has increased collaborative research with other institutions. Examples of collaborative research include instances where the same research study has researchers and/or subjects from multiple institutions, thereby coming under the jurisdiction of multiple IRBs. In effect, Boston Children's IRB has increased efforts to utilize reliance agreements in which one IRB relies upon (cedes to) the review, approval and oversight of another IRB. These agreements help streamline the IRB process for a protocol involving multiple institutions and avoid duplicate oversight from multiple IRBs.

Increased efforts for using IRB reliance agreements at BCH include:

1. IRB Personnel: IRB Specialist Daniel Alderson joined our team in July 2014 with a primary focus on multi-site protocols and reliance agreements. Daniel oversees protocols with multiple institutions where more than one IRB has jurisdiction and is our resource for all reliance agreement processing and management.
2. CHeRP Updates: In March 2015, new activities were created in CHeRP specific to requesting and processing reliance agreements. The 'Reliance on Another IRB' activity can be found as a submission type when submitting a new protocol. It is an abbreviated submission which goes through administrative review. It does not go through a standard IRB review process but rather is a means to track research activities occurring at BCH as well as trigger any applicable non-IRB ancillary reviews. The 'Add Reliance on BCH' activity allows you to add a site (who is relying on BCH IRB via a reliance agreement), its investigators, site-specific consent forms and recruitment documents, etc. to the protocol. An 'Add Reliance on BCH' activity can be opened as long as the main protocol has been submitted. It can be found in the same area where you would submit an Amendment, Continuing Review, etc. and pushes reliance-related information to the main protocol in a similar fashion as an Amendment. In addition, multiple 'Add Reliance on BCH' activities can be opened simultaneously should several institutions be relying on BCH for the same protocol.
3. Reliance Models: BCH IRB uses multiple models of reliance agreements to meet the needs of researchers and their protocols. One example is the use of a central IRB where BCH or another institution acts as the sole IRB for multiple protocols and multiple institutions who may be part of a consortium. Another example is the use of Master Reliance Agreements in which agreements are set up for institutions whose researchers work together frequently and the agreements can be applied for any or all applicable protocols.

Boston Children's Hospital IRB is here to assist in the regulatory needs of multi-site research. If the involvement of multiple sites for your research means multiple IRB review and oversight, consider a reliance agreement to avoid duplication of effort across those sites. Please contact IRB Specialist Daniel Alderson (daniel.alderson@childrens.harvard.edu ; 617-919-1918) for assistance.

Scott Meyers earns Certified IRB Professional (CIP) designation.

Congratulations to Scott Meyers passing the prestigious Certified IRB Professional (CIP) exam! In March, Scott sat for and passed the rigorous 250-question exam which covers all aspects of human research protections, including IRB operations and record-keeping as well as Federal and international regulations and guidelines. Scott's certification represents his commitment to excellence in the field and the breadth of his expertise. CIPs are the elite experts in the human subjects protections field. With his certification, Scott joins fellow BCH IRB staff who have obtained CIPs previously, including Ashley Kuniholm, Susan Corl and Daniel Alderson. Congrats, Scott!

A new view has been created in CHeRP making it easier to locate a protocol's various submissions i.e. Original Protocol, Amendments, Continuing Reviews, Reportable Events, Reliance Agreements, and their associated details in sequential order, in one place. The new Review Summary tab can be found within the main protocol workspace, under the dashboard and to the far right of the protocol tabs (History Log, Sticky Notes, etc.). Review Summary provides a quick summary of each IRB review on the same page. For Amendments, the corresponding proposed modifications are also listed along with an indication as to whether consent changes were made, reducing the need to open each amendment separately to find details of the review.

<u>The review information is displayed as follows:</u>

Submission ID provides the link to open the full submission.

Submission Date lists the date it was submitted by the research team.

Approval Date lists the approval date as a link to open the Report of Action (final approval) letter. When viewing the *Original* submission, the initial Report of Action (final approval) letter will only be available for protocols that were created in CHeRP.

Summary of Changes provides a summary of the *PROPOSED modifications* that were provided by the research team in the Amendment Form. The *IRB-APPROVED modifications* can be found in the Report of Action (final approval) letter for that amendment (via the Approval Date link).

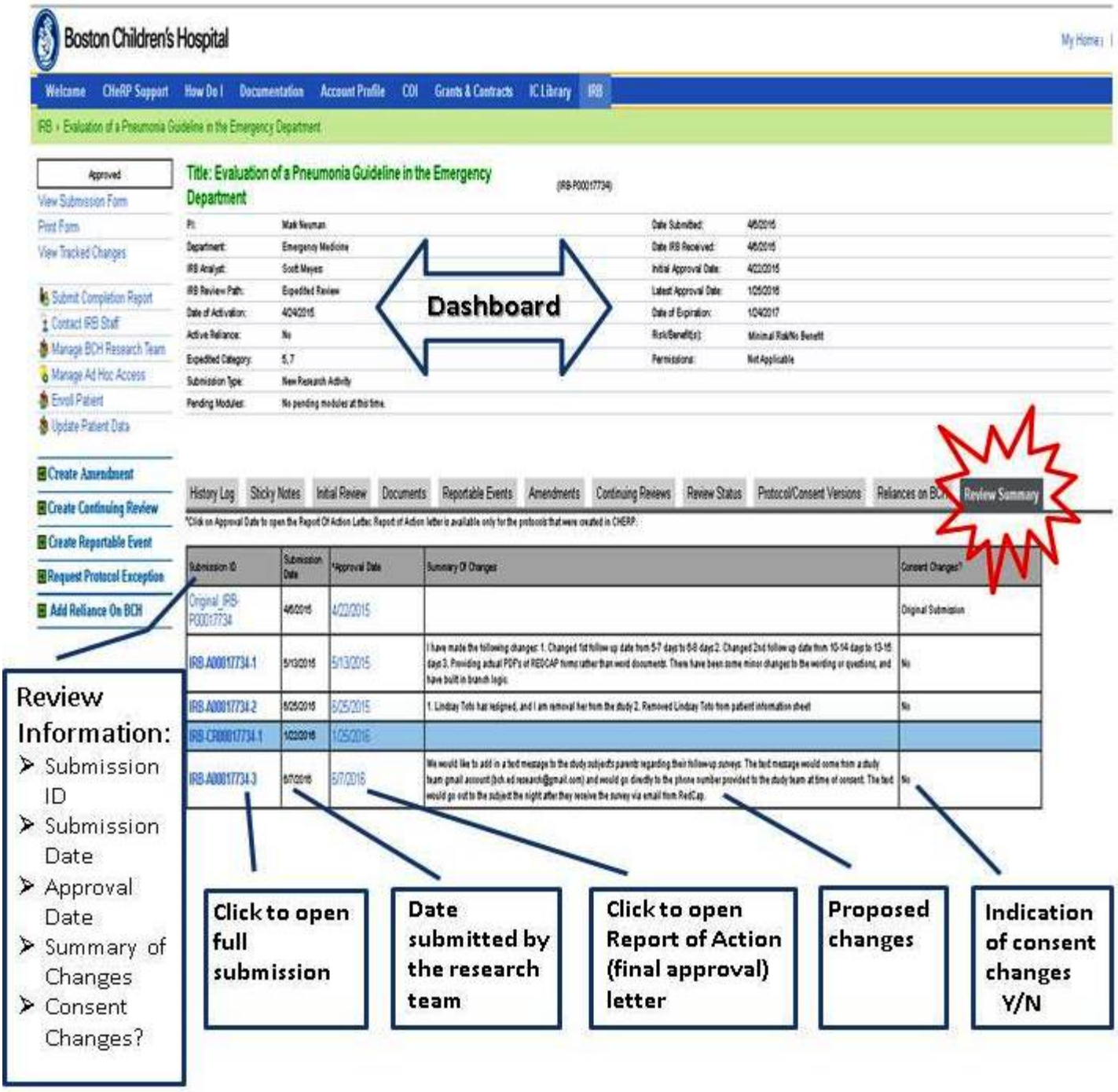
Please note this will only reflect consent changes after June 1, 2016. We are unable to provide this information prior to that date.

Consent Changes?* indicates whether consent changes were made as part of the amendment submission. The actual finalized consent documentation can be located by going to the **History Log** (tab) and searching for the **Consent Forms Finalized** Activity. This may be done by scrolling through the History Log and locating the amendment Approval Date, or clicking the *Activity* link (found directly under "History Log") and doing the same. In the History Log the amendment's Approval Date will correspond to the Activity Date (listed to the far right).

For consent form changes prior to June 1, 2016:

** Please note that information provided in this column is accurate for amendments approved on or after <u>June 1, 2016</u>. If approved prior to this date, the Report of Action (final approval) letter may be referenced for consent changes. If applicable, the finalized consent documentation may then be located by following the aforementioned steps.*

Review Summary Tab: CHeRP view (main protocol workspace)



Memo-to-File: from the EQUIP Office

Could a non-English speaking subject or parent/guardian of a subject participate in your research study?

Regulations require that the informed consent information be presented in a language understandable to the subject and/or parent/guardian of the subject. Please review the following information to ensure that you and your study team understand the steps for obtaining and documenting the consent process for a non-English speaking subject and/or parent/guardian of a subject.

For **greater than minimal risk** research, the consent form must be translated into the appropriate language:

a. Ensure the English consent form is properly translated and approved by the IRB (translated consents must be stamped) and available to subjects and/or their parents/guardians at the time of consent.

b. Ensure a qualified interpreter is involved in the consent process, either in-person (preferred) or remotely (e.g. by phone).

c. Ensure the interpreter's involvement in the consent process is adequately documented with a signed, dated note-to-file, or notation on the consent document.

For **minimal risk** research, the IRB allows the use of the 'short form' method of consent. This method allows a non-English speaking subject or parent/guardian to sign a translated statement (or 'short form') which attests that the elements of the approved English consent have been presented orally by a qualified interpreter, in place of a translated consent form. The 'short form' has been translated in over 2 dozen languages and can be downloaded as needed from the IRB website. Before using the short form method, make sure the IRB approval letter for the study specifies the short form may be used.

a. Ensure a qualified interpreter is involved to orally present the consent information and to ask/answer questions between the subject and PI/person obtaining consent.

b. Ensure required signatures are obtained and properly documented:

i. Non-English speaking subject/parent/guardian must sign and date the translated short form
ii. PI/person authorized to obtain consent must sign the English consent form.
iii. Interpreter or witness must sign both the English consent form and translated short form.

c. Ensure the subject/parent/guardian receives copies of both English consent and translated short form.

More detailed info & resources for translating consents can be found in the IRB Policy: 7.4 Informed Consent with Non-English Speakers.
Please take a few moments to verify that everyone on your study team that who may consent a research subject is familiar with the policy.

Boston Children's Hospital

Boston Children's Hospital
Institutional Review Board (IRB)

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The Institutional Review Board (IRB) has been established to oversee the protection of human research subjects at Boston Children's Hospital. Children's is committed to safeguard the rights and welfare of all children, adolescents, adults and family members who volunteer to participate in research. To this end, the IRB Office upholds the principles of the Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research, as the cornerstone of our mission, organization and daily activities.

- Have questions or comments about any of the articles in this newsletter?
- Need advice about your research?
- Want to know more about human subjects protection at BCH?

Please don't hesitate to contact the IRB Office and one of our staff will be happy to assist you.