Agenda

- ORIO Move to Bancroft – new service model
- Update on Repository Compliance Program
- New Re-Consent Policy
- Policy Update on Obtaining Consent from Minors
- Changes to Federal Liability Language
- Clinical Research Billing Updates
- Expedited Review of Previously collected data
- Changes to Approval Memos
- Treatment Use Options for Drugs
- Early & Expanded Access & HUDs for Devices
ORIO Moving to BANCROFT BLDG!

- Accessible by tram and foot (next to Old Spaghetti Factory)
- Crafting our Outreach & Enhanced Service Plan after the move to Bancroft
  - Continue Annual IRB Town Hall
  - Departmental assignments – lines up a particular analyst per department
  - Maintain 2 analysts per day to answer all general calls – ensures ‘live’ person when researchers call
  - Initial response to inquiries within 24 hours
  - Establish set conference room for all IRB Trainings
    - eIRB 101/201 continue – set certain days per month (1st Tuesday, 2nd Friday, etc.)
    - Analyst Brown Bag Sessions – set on a certain day each month, covers specific topics or open Q&A sessions, may have guest speakers
    - Quarterly eIRB User Group Sessions – designed to gather feedback from users on future development/fixes
Update:
Repository Compliance Program

- Must be compliant with new policy by 8/30/2011

- Goals
  - Compliance with regulatory requirements
  - Maximize utility of resources
    - Facilitating sharing of data/samples
    - Decreasing limits on use
  - Standardize the process institution-wide
  - Decrease ongoing compliance requirements for continuing reviews.
Repository Policy: 
Applicability of the Policy

- This policy applies to human subject research repositories established by OHSU investigators for the purpose of storing data and/or specimens for future research purposes.

- This policy does not apply to data/specimens that are collected and stored as part of routine clinical care or hospital procedures, for example, blood banks, pathology, surveillance, or quality assurance. However it does apply to data/specimens from these sources that are then stored for future research.
Repository Policy: Repository - Defined

- Generally, a repository collects, stores and distributes human tissue, specimens and/or data for use in future research projects. Any collection of human biological materials (including data) is considered to be a repository when there is no explicit plan to destroy the materials when the specific research project that generates the materials ends.

- Registries, data banks, and tissue banks are all considered “repositories” for regulatory purposes. Any reference in this policy to repositories applies equally to data banks, tissue banks, and registries.
Repository Policy:
The Basics of a Repository

- Repository activities involve three components:
  - 1) the collection of materials,
  - 2) the repository storage and data management
    and
  - 3) the use by recipient investigators.
Repository Policy: Submitting for IRB Approval

- The electronic IRB (eIRB) contains a specific application for the creation of new research repositories.

- Any existing study that is completed but has collected data and/or specimens for future research purposes may choose to convert the study to a repository via a modification or continuing review application.

- It is recommended that a request for determination be sought from the OHSU IRB whenever there is a question of IRB oversight requirements.
What about industry-sponsored studies that store with the sponsor?

- This is not a repository that requires specific IRB review. The activity is covered in the study-specific review.

OHSU’s general policy is to assume that all storage of samples for future research may include genetic research and therefore, we include language to facilitate future genetic research. What if the sponsor insists that genetic research will not occur?

- We believe them. The contract supports it.
## Update: Repository Compliance Program

<table>
<thead>
<tr>
<th>#</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>33</td>
<td>New Repository Only Submissions (this does not include pre-existing repositories that had used the old study path to gain approval)</td>
</tr>
<tr>
<td>85</td>
<td>The # of studies that now have IRB approval to ‘include a repository’ as part of their study submission</td>
</tr>
<tr>
<td>432</td>
<td>The # of IRB approved studies that indicate they are storing data or samples for a repository but have yet to receive IRB approval. (in various states of ACTIVE (234*), Closed to Enrollment, all the way down to researcher preparation)</td>
</tr>
<tr>
<td>*234 (out of the 432 listed above)</td>
<td>Currently ACTIVE studies that <strong>still need to begin</strong> the process of coming into compliance (they have not yet completed a CRQ or MRQ to answer the repository questions)</td>
</tr>
<tr>
<td>~60 (out of the 432 listed above)</td>
<td>Are in the process of receiving approval (in various states; pre board revisions, analyst review, board review, etc.)</td>
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<tr>
<td>~70 (out of the 432 listed above)</td>
<td>These are brand new studies that are in ‘researcher preparation’ and have indicated some sort of repository element in the IRQ but have yet to be submitted to the IRB.</td>
</tr>
<tr>
<td>963</td>
<td>The # of studies that have completed CRQs and have received approval from the IRB indicating that they have no intention of storing for future use and their protocols confirm that they will not be storing.</td>
</tr>
<tr>
<td>322</td>
<td>The # of IRB approved studies whose CRQs have been submitted but the answers to the repository questions do not match up with what they have indicated in the IRQs and therefore will need to be clarified one way or the other. Our analyst teams will be contacting these investigators for follow up information.</td>
</tr>
<tr>
<td>????</td>
<td>The # of repositories that exist and the PI doesn’t know that the repository is subject to the law and the OHSU research repository policies</td>
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New Policy: Re-Consent or Notification Due to New Information or Changes

- The IRB may permit or require re-consent or notification of subjects when significant new information or changes arise during the course of the research, that may relate to the subject’s willingness to continue participation.

- Examples of such information include:
  - Findings of increased risk to subjects;
  - Addition of new procedures requiring more intervention/interaction with subjects;
  - New uses of subject data or specimens that do not otherwise qualify for a waiver of consent;
  - Evidence that the study treatment may not be as effective as originally anticipated or that another treatment may be available;
  - Significant changes in study schedule; and/or
  - Significant changes in investigator conflicts of interest
In some cases where new information arises during or after the research has begun, full re-consent may not be necessary or appropriate. Written or verbal notification to subjects or no action at all may be acceptable. In determining the methods to be used to provide subjects with new information, the IRB may consider a variety of factors, including:

- The significance of the information and the likelihood that it might affect subjects’ willingness to continue participation
- The subjects’ progress in the research (e.g. active study treatment vs. long-term follow-up)
- Whether there is a possibility of intervention (now or in the future) based on the new information
- Whether re-consent would require unnecessary inconvenience for subjects and/or excessive administrative burden for study staff
- Whether re-consent might create additional anxiety for subjects
Re-Consent Policy:
Submitting a Modification

- Investigators becoming aware of new information related to study participation should evaluate the information and make an initial determination as to the need for re-consent or notification and the format that the communication should take.

  - The investigator should submit a modification via the eIRB that includes all changes to study documents and procedures based on the new information.

  - A plan for re-consent or subject notification, or justification for taking no action, should be included with the modification.

  - If any subjects have already been informed of any of the new information, the investigator should provide a summary of the communications.
Re-Consent Policy:

IRB Review

- The IRB will consider the investigator’s proposed plan when considering whether to approve the modification. The IRB may require changes to the plan based on consideration of the previously listed factors and any other relevant considerations. Specific IRB requirements regarding the re-consent or notification process will be stated in the review communication.

- Sponsors may require re-consent even when the IRB may not otherwise require it. If the sponsor requires re-consent, the investigators should notify the IRB at the time the modification is submitted. The IRB may permit re-consent even if the IRB finds it unnecessary.
Re-Consent Policy:
Notification without prior IRB Review

- In rare occasions, the time for IRB review may unacceptably delay communication of new information to subjects.
- Investigators are authorized to act in the best interest of subjects with regard to relaying new information to subjects prior to IRB approval.
  - If an investigator finds it appropriate due to the critical nature of the new information, subjects may be contacted and informed at the next reasonable opportunity, and given an opportunity to withdraw from the study.
  - If feasible, the IRB must be notified prior to such action. If the PI feels it is in the best interest of research subjects to notify subjects immediately of the new information, then the IRB should be notified via “contact IRB” function in the elIRB.
Re-Consent Policy:
Methods for Re-Consent/Notification

- **Re-consent using an updated version of the original consent form.** This is the most complete method of re-consent and is best reserved for extensive changes to the study design, procedures, or risks. A cover letter and/or a system for showing subjects what has changed (e.g. highlighting new information) may help improve subject comprehension.

- **Re-consent using an addendum to the original consent form.** This may be useful when new information is limited to a relatively narrow topic, such as new or modified risks. It gets quickly to the point and avoids burdening the subject with the entire consent form when most of it is unchanged. For studies that are actively enrolling, the original consent form will still need to be updated.
Re-Consent Policy:
Methods for Re-Consent/Notification

- **Re-consent using a letter with signature.** When subjects are not scheduled for an in-person visit and the nature of the information does not necessitate a personal conversation (because it’s a clear or simple change or little action is required), researchers may send subjects a letter and ask them to return a signed acknowledgement. The letter should include a contact phone number that subjects may call if they have questions.

- **Oral Re-consent.** Generally, subjects may be verbally informed of new information and asked if they wish to continue participating in the study in situations where the requirement to document informed consent has been waived. Oral re-consent may also precede written re-consent when necessary to relay time-sensitive critical information to subjects.

- **Notification via letter or conversation.** Information unlikely to change a subject’s willingness to participate in the study may not warrant re-consent. Oral or written notification, depending on the circumstances (such as whether the subject is scheduled for a visit in the near future), may be sufficient.
Policy Update:
Consent for 15-17 year olds

- The OHSU IRB will allow the application of the State law related to the age at which individuals under the age of 18 may seek care without parental consent.

- Generally, when children cannot legally give consent, informed consent must be obtained from parents ("parental permission"), or the legally appointed guardian.
Consent for Minors (15-17) in Research Policy:

- Under Oregon law, minors may consent to participation in research without parental or guardian permission (i.e., as if adults) if legally emancipated and in certain treatment circumstances.

Consent for Minors (15-17) in Research Policy:

- OHSU interprets laws regarding emancipated minors and married minors as authorizing a minor to consent to research as an adult does. This applies for any type of research.

- In Oregon, the “treatment” laws generally apply to medical care, substance abuse treatment and reproductive health care. Therefore, minors aged 15-17 can consent to research providing such treatment.

- For research involving activities that are not specifically indicated in the Oregon State laws, individuals under the age of 18 are considered minors and may not consent to research.
Consent for Minors (15-17) in Research Policy: Parental Involvement

- Even though Oregon law and OHSU policy allow for minors to provide legally effective informed consent in certain situations, obtaining consent from a parent or guardian is still the best practice in most cases.

- Parental Notification – Oregon allows for disclosure to the parents of the non-emancipated minor’s consent in cases of mental health or chemical dependency treatment and general medical and dental care. If parents are going to be advised on the child’s consent to care, then the plan must be described in the protocol and addressed in the consent form.
Consent for Minors (15-17) in Research Policy: Signatures

- Consent Form Signature Templates for Children Ages 15-17
  [Link](http://www.ohsu.edu/xd/about/services/integrity/policies/policy-detail.cfm?policyid=1889754)

- If you intend to seek consent from a parent or guardian for the minor’s participation, use **signature page option #1** - Note that 15-17 year old subjects are also asked to document their own consent on this page via a second signature line.

- Assent for subjects ages 7-14 (or older, if appropriate in light of the specific study circumstances or the nature of the subject population) should still be documented using the OHSU standard assent form or an assent form drafted specifically for your study.

- If you believe that obtaining parent/guardian consent is not the best practice for your study and the subjects may legally consent for themselves, you may use signature page option #2.

- For this, you should submit a memo to the IRB that:
  - Explains your rationale, and
  - Describes any plan to involve parents/guardians in the subjects’ study participation where appropriate.

- You will note the presence of a parent/guardian acknowledgment signature line on this page. Whether you should have the parent/guardian sign the consent form depends on the nature of the study and the individual subject’s circumstances. Generally, the IRB will defer to researcher discretion regarding when parent involvement in a study is appropriate.
Consent for Minors (15-17) in Research Policy: Signatures ~ 2 Options

Option #1: Use this page for studies where parent/guardian consent will be sought. For studies that involve a minor increase over minimal risk with no prospect of direct benefit to the subject (child category 406), ADD A SECOND parent/guardian signature line.

Your signature below indicates that you have read this entire form and that you agree to be in this study.

_____________________________  ______________________
Signature of Subject                      Date
(or Parent/Guardian if subject is under 18)

_______________________________
Printed Name of Subject
(or Parent/Guardian if subject is under 18)

_______________________________  ______________________
Signature of Person Obtaining Consent                      Date

_______________________________
Printed Name of Person Obtaining Consent

Subjects ages 15-17:

Your signature below indicates that you agree to be in this study.

_____________________________  ______________________
Signature of Subject                      Date

_______________________________
Printed Name of Subject

OPTION #2: Use this page for studies involving research-related treatment and/or provision of clinical care where researchers request that parent/guardian consent not be required.

Your signature below indicates that you have read this entire form and that you agree to be in this study.

_____________________________  ______________________
Signature of Subject                      Date

_______________________________
Printed Name of Subject

_______________________________  ______________________
Signature of Person Obtaining Consent                      Date

_______________________________
Printed Name of Person Obtaining Consent

Parent or Guardian Signature for Subjects age 15-17 (if applicable):

Your signature below indicates that you have been informed about your child’s participation in this study and your anticipated involvement as a parent or guardian.

_____________________________  ______________________
Parent/Guardian Signature                      Date

_______________________________
Printed Name of Parent/Guardian
Change to CF Liability Language for Federally Funded Studies

- **The OLD language:** “It is not the policy of the federal funding agencies to compensate or provide medical treatment for human subjects in federally funded studies.”

- **Must be REPLACED with:** “This federally funded study does not have the ability to provide compensation for research-related injury. If you are injured or become ill from taking part in this study, it is important to tell your study doctor. Emergency treatment may be available but you or your insurance company will be charged for this treatment.”
New studies must use the new liability language. If your study has already been submitted and initial review is in process, the Institutional Review Board (IRB) will update the language for you.

Approved studies must update their liability language at the next continuing review. You may also update it as part of a modification before your next continuing review, but you are not required to submit a modification solely for this purpose.

Note: Subjects already enrolled in federally funded studies DO NOT need to be re-consented and sign the updated consent form.
Clinical Research Billing Update

- Clinical Research Billing Office (CRBO)
  - Director – Melanie Hawkins
  - http://www.ohsu.edu/xd/research/about/integrity/irb/clinical-research-billing.cfm?WT_rank=1

- New Clinical Research Billing form as of 12/1/2010

- New Consent Form Cost Language
  - The costs language has been standardized and moved to a separate document, similar to the liability language.
  - Follow the link in the consent template you are using to reach the new document, or locate the new "Costs Language" document on the forms page. Select the option that applies to your study, copy it, and paste it into your consent form.
  - Required 6/1/2011
Expedited Review of Data previously Collected for Research Purposes

- **Category 5**
  - Research involving materials (data, documents, records, or specimens) that have been collected, or
  - will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

- May now be expedited rather than going to full board for review.
Changes to Approval Memos

- Change to come:
  - Only Industry-Sponsored studies will have a list of items reviewed and approved in the memo.

- Why the change?
  - Not a required element to list them individually
  - Avoids errors and unnecessary work
Access to Investigational Drugs Outside of a Clinical Trial

- Patients may be eligible to receive an investigational drug as a participant in a clinical trial or as part of an expanded access program.

- Expanded access, sometimes called "compassionate use," is the use of an investigational drug outside of a clinical trial to treat a patient with a serious or immediately life-threatening disease or condition who has no comparable or satisfactory alternative treatment options.

- [http://www.ohsu.edu/xd/about/services/integrity/policies/irb-policies-fda-research.cfm](http://www.ohsu.edu/xd/about/services/integrity/policies/irb-policies-fda-research.cfm)
Mechanisms for Treatment Uses for Investigational Drugs

- New Rules in 2009
- Expanded access to investigational drugs for treatment use will be available to:
  - Individual patients, including in emergencies, on a case-by-case basis. Limited number of uses. — reported to IRB, preferable before use.
  - Intermediate-size patient populations with similar treatment needs who otherwise do not qualify to participate in a clinical trial. (smaller than those typical of a treatment IND or treatment protocol) — regular IRB review and approval
  - Under a treatment protocol or treatment investigational new drug application (IND) for larger populations who do not have other treatment options available, once more is known about the safety and potential effectiveness of a drug from ongoing or completed clinical trials — regular IRB review and approval
Early & Expanded Access to Devices

- An unapproved medical device may normally only be used on human subjects through an approved clinical study in which the subjects meet certain criteria and the device is only used in accordance with the approved protocol by a clinical investigator participating in the clinical trial.

- There may be circumstances under which a health care provider may wish to use an unapproved device to save the life of a patient or to help a patient suffering from a serious disease or condition for which there no other alternative therapy exists.
Early & Expanded Access to Devices

- **Emergency Use** –
  - Life-threatening or serious disease or condition
  - No alternative
  - No time to obtain FDA approval - Emergency use of an unapproved device may occur before an IDE is approved.
  - May be Before or after initiation of the clinical trial
  - Information about use submitted to IRB, preferably before use.

- **Compassionate Use (or Single Patient/Small Group Access)**
  - Serious disease or condition
  - No alternative
  - Prior FDA approval is needed before compassionate use occurs
  - This occurs concurrently with a clinical trial setting – Get IDE Supplement
Early & Expanded Access to Devices

- **Treatment Use**
  - Life-threatening or serious disease
  - No alternative
  - Controlled clinical trial – Regular IRB Review and Approval Required.
  - Sponsor pursuing marketing approval

- **Continued Access** –
  - FDA allows continued enrollment of subjects after the controlled clinical trial under an IDE has been completed in order to allow access to the investigational medical device
  - Regular IRB Review and Approval Required
What about Humanitarian Use Devices?

- A HUD is a “medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4,000 individuals in the United States per year.”

- A Humanitarian Device Exemption (HDE) is an application that is similar to a premarket approval (PMA) application, but is exempt from the effectiveness requirements.

- “Use” of HUD may be for treatment or in a clinical investigation.
  - Special IRB approval is required before a HUD is used at a facility to treat or diagnose patients and the IRB requires informed consent.
  - Regular IRB review and approval is required for investigational uses of HUDs.
  - Just because an IRB has approved use of a HUD at a facility to treat or diagnose patients does **not** mean that the IRB has approved investigational use of the HUD (i.e., in a clinical investigation), for the collection of safety and effectiveness data.
Questions?

Thanks!

- **Research** is:
  - "A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." [45 CFR 46.102(d)]

- **Human Subjects** is:
  - "...living individual(s) about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information." [45 CFR 46.102(f)(1-2)]