State of the IRB
Important News

- AAHRPP Accreditation!
- Two new IRB chairs:
  - Caren Frost, PhD – College of Social Work
  - Richard Lemons, MD – Pediatrics
- Farewell to Drs. Ingrid Nygaard and Dennis O’Rourke
  - Reception at the IRB: Friday, 10/30/2015 @ noon
The number of active studies is an average taken at four points in time during each year.
Number of New Studies Approved Each Year, By Review Type

- Convened Board
- Expedited Review
- Exempt Review
- Administrative Review
Number of New Studies Approved Each Year, by Study Location

- **UUHSC**: 605, 625, 648, 700, 721, 818, 848, 871
- **UMain**: 322, 353, 336, 375, 318, 389
- **PCH**: 78, 87, 100, 109, 93, 84
- **VA**: 57, 36, 67, 53, 43, 55
- **P+UUHSC**: 55

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<td>1.</td>
<td>Pediatrics (includes Peds Onc)</td>
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<td>Internal Medicine</td>
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<td>Nursing</td>
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<td>Adult Oncology</td>
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<td>Pharmacy +2</td>
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<td>Surgery -1</td>
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<td>Orthopedics -1</td>
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<td>8.</td>
<td>Neurology +1</td>
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<td>Psychology +3</td>
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<td>OB/GYN -2</td>
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<td>11.</td>
<td>Ed Psychology +14</td>
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<td>12.</td>
<td>Communication +7</td>
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<td>13.</td>
<td>Exercise and Sport Science -3</td>
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<td>14.</td>
<td>Gastroenterology +3</td>
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<td>15.</td>
<td>Family and Preventive Medicine +1</td>
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<td>Medical Informatics +4</td>
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<td>Social Work -6</td>
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<td>Dermatology +2</td>
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Number of Active Studies, by College/Department/Division
(Top 10)
June 3, 2015

- Pediatrics: 678
- Adult Oncology: 434
- Internal Medicine: 432
- Surgery: 198
- OB/GYN: 176
- Nursing: 167
- Orthopedics: 166
- Pharmacy: 164
- Psychology: 148
- Neurology: 146
Notice of Proposed Rulemaking (NPRM) Highlights
Expand the Definition of Human Subject for De-Identified Biospecimens

- Require informed consent for most secondary research with biospecimens, even when the biospecimens are not identifiable, but through broad consent
- Change the requirements for waiving consent
- The new consent requirement could be met by using a new “broad consent” form to be released by federal government
Mandated Single IRB Review for Cooperative Research

- Institutional Authorization Agreements and Reliance Agreements
- Local Context
- Problem and Event Reporting
- Exceptions
- Potential Consequences
Non Human Subject Research, Exempt and Excused Categories

- Program Improvement, Oral History, Journalism, Biography, QA/QI, Public Health Surveillance
- Exclusion of Educational Tests, Surveys, Interviews, Observation of Behavior
- Exempt Decision Tool
- Investigators can determine whether a project is exempt
NPRM Highlights

Questions/Discussion
University of Utah
Annual IRB Member Training
October 0215

Return of Incidental Genetic Findings
IRB Working Group

- Jeff Botkin, MD
- Dave Viskochil, MD
- Deb Nekalson, PhD
- Hilary Coon, PhD
- Neil Bowles, PhD
- Brian Watts, JD
Investigator Consultations

- 3 study teams, including investigators, study coordinators, data analysts, and genetic counselors
New & Updated Information

- Updated guidance to include WGS/WES
- Added a standard institutional process for disclosure
- Added consent language for potential return of incidental genetic findings
- Added a new application page to ERICA for Genetic Research
CLIA vs. HIPAA

- CLIA requires no disclosure of results unless testing is performed in a CLIA-approved lab.
- HIPAA requires patients to have access to information in their medical/health record, including research data.
Breadth of Researcher Responsibility

- Investigators are not expected or required to complete exhaustive genetic testing to identify all possible, known genetic variants as part of the research.
- It may be appropriate to exclude analysis of variants that are irrelevant to the research objectives.
- Research to clinical hand-off should be made.
- Costs of clinical re-testing may be born by the participant.
1. Ensure that the approved protocol and consent document(s) allow for disclosure of results and incidental findings to participants and/or affected family members.
In this research, we are only looking for changes in your genes that are related to <<condition under study>>. But it is possible that we may come across changes in your genes that are related to other health conditions. These other findings may be important to your health care or the health care of your family members.

If this happens, we may contact you to give you a choice about learning about these findings. We will also refer you to a genetic counselor who can help you make a decision and talk to you about how you might use the results in your health care.

In this study about <<condition under study>>, we are not looking for results related to other conditions. This means that you might have changes in your genes related to other health conditions that we will not identify in this study.

In most cases we may need to retest your original blood sample or obtain a new sample for clinical testing. We may refer you to clinical specialists where retesting could be done to verify results. If you choose to receive results, the cost of clinical retesting may be billed to your insurance or you.
- Risks, privacy, confidentiality add-on questions
- Will incidental findings relevant to individuals or families be communicated to the participants? *If yes:*
  - Describe the process for determining which incidental findings will be returned to the participants. Describe the information and expert consultation that will be used to make this determination.
  - Indicate the process that will be used to return information about incidental findings to participants:
    - Standard institutional process (with hyperlink)
    - Other: [describe]
2. Determine the appropriateness of disclosing genetic information to participants and/or affected family members. Consider:

- Evidence of clinical application
- Age of affected participants
- Legal considerations
3. Begin process of discussion and disclosure with the participant. This process must be conducted by a genetic counselor or other trained professional who can discuss the implications of genetic findings.
   a. Initial contact
   b. Pre-test counseling appointment
   c. Post-test counseling appointment
Initial Contact

- Made by phone, in person, in writing.
- Indicate that there is an incidental finding and gives the participant the option to learn more.
- Present general information about the finding: “This result could have implications for your risk of cancer/heart disease/etc.”
- Schedule a pre-test counseling appointment.
Pre-test Counseling Appointment

- Discuss research finding with the participant and the need for clinical testing in a CLIA-approved lab.
- Discuss costs of testing, including billing to insurance.
- Participant provides standard clinical consent for testing.
- Samples for testing are taken; testing is performed.
Post-test Counseling Appointment

- Discuss the clinical results with the participant.
- Additional referrals for medical care and follow-up may be made as part of standard of care.
Deviations from the Standard Process

- Investigators can propose a different process in the IRB application.
- The IRB will need to consider whether a different process is appropriate, given the population and the circumstances of the study.
Questions or Comments?

Thank you!

IGS: Genetic Research
Placebo Studies with Children
Final FDA Rule: Additional safeguards for Children in Clinical Investigations

- Released in February 2013
- No changes to the FDA regulations
- Changes to FDA guidance...Importantly, changes to how direct benefit to children should be considered.
Old way of thinking...

- Possible direct benefit to children in research may come from increased monitoring and care of participants, even though a child may not actually receive a test product.
“...the so-called ‘inclusion’ benefit is not a ‘direct’ benefit...children enrolled in the placebo arm of a trial should be exposed to no more than a minimal risk or a minor increase over minimal risk.”

“The interventions that do and do not offer a prospect of direct benefit in any given protocol must be analyzed separately (often called a component analysis of risk).”
“[P]lacebo-controlled trials are acceptable in situations where there are no approved or adequately studied therapies for children with the condition under study.”
Implications for the IRB

- Separate Children Determinations for treatment arm(s) and placebo arm(s)
  - Updated IRB Member Checklist to allow for multiple category selection
- The majority of placebo studies with children at the UUHSC/PCH add the investigational treatment/placebo to usual standard of care → most placebo arms will be considered minimal risk, if there are no additional research procedures
  - More than minimal risk procedures: MRIs with gadolinium or sedation, frequent/high volume blood draws, radiation exposure, lumbar punctures, additional biopsies
Questions or Comments?

Thank you!

Additional Safeguards for Children in Clinical Investigations of Food and Drug Administration-Regulated Products

- Federal Register / Vol. 78, No.38 / Tuesday, February 26, 2013
University of Utah
Annual IRB Member Training
October 2015

Planned Emergency Research
What is Planned Emergency Research?

- Planned emergency research involves the systematic investigation of a condition experienced by individuals "in a setting where the emergency circumstances require prompt action and generally provide insufficient time and opportunity to locate and obtain consent from each subject's legally authorized representative" (FDA 2013).
- Because informed consent cannot be obtained prior to initiating research procedures, there are many additional participant protections that must be in place before the IRB can approve planned emergency research.
Examples of Planned Emergency Research Conducted at UUHSC/PCH

- A Phase III, Randomized, Controlled, Open-Label, Multicenter, Parallel Group Study Designed to Evaluate the Safety and Efficacy of Poly SFH-P Injection [Polymerized Human Hemoglobin (Pyridoxylated), PolyHeme] When Used to Treat Patients in Hemorrhagic Shock Following Traumatic Injuries Beginning in the Prehospital Setting
- Use Of Lorazepam For The Treatment Of Pediatric Status Epilepticus: A Randomized, Double-Blinded Trial Of Lorazepam And Diazepam
- Established Status Epilepticus Treatment Trial (ESETT)
- Study of Tranexametic acid during Air Medical Prehospital transport (STAAMP) trial
Additional Protections and Requirements

1. Justification for planned emergency research design *
2. Informed consent process with the participants and/or their legally authorization representatives (LARs) *
3. Community consultation and public disclosure *
4. Establish an independent data and safety monitoring board (DSMB)
5. Obtain an IND or IDE from the FDA
1. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.
2. Obtaining informed consent is not feasible because:
   - the subjects will not be able to give their informed consent as a result of their medical condition;
   - the intervention involved in the research must be administered before consent from the subjects' legally authorized representatives is feasible; and
   - there is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.
3. Participation in the research holds out the prospect of direct benefit to the subjects because:

- subjects are facing a life-threatening situation that necessitates intervention;
- appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
- risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
1. The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each participant within that window of time and, if feasible, asking the legally authorized representative contacted for consent within that window rather than proceeding without consent.

2. The investigator has summarized efforts that will be made to contact and obtain consent from legally authorized representatives as soon as possible upon identification of an eligible participant and make this information available to the IRB at the time of continuing review.
3. If obtaining consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the participant’s family member who is not a legally authorized representative, and asking whether he or she objects to the participant’s participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
4. If a legally authorized representative or family member is told about the clinical investigation and the participant’s condition improves, the participant is also to be informed as soon as feasible.

5. If a participant is entered into a clinical investigation with waived consent and the participant dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the participant’s legally authorized representative or family member, if feasible.
Community Consultation & Public Disclosure

- An appropriate plan for consultation with representatives of the communities in which the clinical investigation will be conducted and from which the participants will be drawn.
- An appropriate plan for public disclosure to the communities in which the clinical investigation will be conducted and from which the participants will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits.
- An appropriate plan for public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results.
Goals of Community Consultation

Two-way communication between the community and the researcher.

- show respect for persons by informing the community about the study in advance;
- inform community members about the trial in advance and provide a means for affected communities to provide meaningful input to the IRB before its decision to approve, require modifications to, or disapprove the study;
- show respect for the community by allowing representatives of the community to identify potential community-level concerns and effects of the research; and
- show respect for subjects’ autonomy. Respect may be shown by including in community consultation activities individuals who may have, or be at risk for, the condition under study (and thereby obtain input from a group that is expected to be similar to the eventual study subjects).
Goals of Public Disclosure

One-way communication from the researcher to the community.

- provide sufficient information to allow a reasonable assumption that the broader community is aware of the plans for the investigation, its risks and expected benefits, and the fact that the study will be conducted without obtaining informed consent from most study subjects.
- ensure that the communities, the public, and scientific researchers are aware of the study’s results.
Implications for the IRB

- Must determine that all 5 protections are in place and meet appropriate standards.
  - IRB Member Checklist: [http://irb.utah.edu/_doc/Reviewer%20Checklist%20%3F%20Request%20for%20Waiver%20of%20Informed%20Consent.docx](http://irb.utah.edu/_doc/Reviewer%20Checklist%20%3F%20Request%20for%20Waiver%20of%20Informed%20Consent.docx)
- May need to give initial approval for beginning the community consultation plan, then review the results of the community consultation plan before giving approval to begin enrollment.
- Participate in community consultation events when possible.
- Give additional consideration of the informed consent process at continuing review, including review of a summary of efforts made to contact a participant’s family members in the event that an LAR was not identified to provide informed consent.
Thank you!

Guidance on Planned Emergency Research

- University of Utah: [http://irb.utah.edu/guidelines/fda-requirements/planned-emergency-research.php](http://irb.utah.edu/guidelines/fda-requirements/planned-emergency-research.php)
FDA Guidance: Mobile Medical Applications
An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—

- recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes (21 U.S.C. 321(h)).
Definitions for Mobile Medical Apps (MMAs)

- **Mobile Platform** = commercial off-the-shelf computing platforms that are mobile
- **Mobile Application (App)** = a software application that can be run on a mobile platform, or a web-based software application that is tailored to a mobile platform
- **Mobile Medical App** = A medical device that is intended (a) to be used as an accessory to a regulated medical device; or (b) to transform a mobile platform into a regulated medical device.
“When the intended use of a mobile app is for the diagnosis of disease or other conditions, or the cure, mitigation, treatment, or prevention of disease, or is intended to affect the structure or any function of the body of man, the mobile app is a [medical] device.”

“Some mobile apps may meet the definition of a medical device but because they pose a lower risk to the public, FDA intends to exercise enforcement discretion over these devices (meaning it will not enforce requirements under the FD&C Act).”
Mobile Apps that are NOT Medical Devices

- Apps that provide access to electronic copies of medical textbooks or other reference materials.
- Apps used as educational tools for medical training or to reinforce training previously received.
- Apps for general patient education and to facilitate patient access to commonly used reference information.
- Apps to automate general office operations in a healthcare setting and are not used to diagnose, cure, mitigate, treat, or prevent disease.
- Apps that are generic aids or general purpose products, such as calculators, audio/video recorders, maps.
Help patients (i.e., users) self-manage their disease or conditions without providing specific treatment or treatment suggestions;

- Provide patients with simple tools to organize and track their health information;

- Provide easy access to information related to patients’ health conditions or treatments;

- Help patients document, show, or communicate potential medical conditions to health care providers;

- Automate simple tasks for health care providers;

- Enable patients or providers to interact with Personal Health Record (PHR) or Electronic Health Record (EHR) systems; or

- Intended to transfer, store, convert format, and display medical device data in its original format from a medical device.
Examples:

- Apps that coach patients with conditions such as cardiovascular disease, hypertension, diabetes or obesity, and promote strategies for maintaining a healthy weight, getting optimal nutrition, exercising and staying fit, managing salt intake, or adhering to pre-determined medication dosing schedules by simple prompting.

- Apps that provide simple tools for patients with specific conditions or chronic disease (e.g., obesity, anorexia, arthritis, diabetes, heart disease) to log, track, or trend their events or measurements (e.g., blood pressure measurements, drug intake times, diet, daily routine or emotional state) and share this information with their health care provider as part of a disease-management plan.
Examples:
- Apps that do not provide recommendations to alter or change a previously prescribed treatment or therapy
- Apps that use a patient’s diagnosis to provide a clinician with best practice treatment guidelines for common illnesses or conditions such as influenza
- Apps that are drug-drug interaction or drug-allergy look-up tools
- Apps that serve as videoconferencing portals specifically intended for medical use and to enhance communications between patients, healthcare providers, and caregivers
Examples:

- Apps specifically intended for medical uses that utilize the mobile device’s built-in camera or a connected camera for purposes of documenting or transmitting pictures (e.g., photos of a patient’s skin lesions or wounds) to supplement or augment what would otherwise be a verbal description in a consultation between healthcare providers or between healthcare providers and patients/caregivers.

- Apps that perform simple calculations routinely used in clinical practice, such as BMI, Mean arterial pressure, APGAR score, NIH Stroke Scale, Delivery date estimator, etc.
MMAs of Regulatory Focus

Mobile apps that are an extension of one or more medical devices by connecting to such device(s) for purposes of controlling the device(s) or for use in active patient monitoring or analyzing medical device data.

- Example: apps that provide the ability to control inflation and deflation of a blood pressure cuff through a mobile platform and mobile apps that control the delivery of insulin on an insulin pump by transmitting control signals to the pumps from the mobile platform.
Mobile apps that transform the mobile platform into a regulated medical device by using attachments, display screens, or sensors or by including functionalities similar to those of currently regulated medical devices. Mobile apps that use attachments, display screens, sensors or other such similar components to transform a mobile platform into a regulated medical device are required to comply with the device classification associated with the transformed platform.
Example: a mobile app that uses a mobile platform for medical device functions, such as attachment of a blood glucose strip reader to a mobile platform to function as a glucose meter; or attachment of electrocardiograph (ECG) electrodes to a mobile platform to measure, store, and display ECG signals.
Mobile apps that become a regulated medical device (software) by performing patient-specific analysis and providing patient-specific diagnosis, or treatment recommendations. These types of mobile medical apps are similar to or perform the same function as those types of software devices that have been previously cleared or approved.

- Example: apps that use patient-specific parameters and calculate dosage or create a dosage plan for radiation therapy
Implications for the IRB

- If a study uses an MMA that is not a medical device, the IRB application should say ‘no’ to ‘Is this the investigational use of a device?’ No device determination needed.
- If a study uses an MMA that is on the enforcement discretion list, the IRB application should say ‘no’ to ‘Is this the investigational use of a device?’ No device determination needed.
If a study uses an MMA that is on the regulatory focus list, the IRB should say ‘yes’ to ‘Is this the investigational use of a device?’ Requires a device determination.
Thank you!

FDA Guidance: Mobile Medical Applications; February 9, 2015
http://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf