RESEARCH COMPLIANCE AND INTEGRITY

Research Compliance and Integrity Hot Topics Session
September 21, 2022
UC San Diego

RESEARCH COMPLIANCE AND INTEGRITY

- Conflict of Interest (COI)
- Dual Use Research of Concern (DURC)
- Export Control and Facility Security
- Institutional Animal Care and Use Committee (IACUC)
- Research Ethics and Integrity (Research Misconduct)
- ClinicalTrials.Gov, NIH Good Clinical Practices (GCP) and Responsible Conduct of Research (RCR) Compliance
- General Research Compliance Activities

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Study Coordinator 102

Study Start-up & Reportable Events

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Brief Into / Background

Michaela Doering, BS
- 25 years in private clinics and pharmaceutical industry: Agouron, Pfizer, Ligand, and Eisai
- Clinical Trials (site level), Clinical Informatics, Medical Writing, and Regulatory
  - Oncology Focused
- 2010 - 2012 - Regulatory Associate, GI Oncology Disease Team at UCSD Moores Cancer Center Clinical Trials Office
- 2012 - present - UCSD MCC Clinical Trials Office, Regulatory Manager
- Piloted use of DocuSign Part 11 for research, reliance IRB programs, and central IRBs
- Works with OIA, PRMC, IBC, and HERC on clinical research policy and practices

Sarah Lazar, MPH
- 2008 - Started at UCSD, Moores Cancer Center
- 2009-2018 - SRA, then Clinical Research Program Manager, Dept of Surgery
- 2018 - present - Clinical Research Manager, Division of Neonatology, Dept of Pediatrics
- Piloted many UCSD research programs, such as Velos
- Interested in improving UCSD-RCHSD research affiliation, and access to resources
Disclaimer

This presentation has been written in reference to the UCSD IRB, Office of IRB Administration (OIA), and their Standard Operating Policies and Procedures (SOPPs).

Please always refer to the policies and SOPs for the IRB of record. Practices and definitions may differ between IRBs.
Clinical Trials - High Level Overview

- Site Qualification
  - CDA/NDA
    - Internal Approval Processes
      - DUA, MTA
        - Contract, Budget
          - IRB Submission
            - Coverage Analysis
              - Regulatory Documents
                - Conflict of Interest
                  - RCHSD PSA*
                    - RCHSD Project Initiation*
                      - Velos/EPIC Research
                        - Invoicing, Reconciliation
                          - Continuing Reviews (as needed)
                            - Final Payment/Closeout
                              - Study Closure
Training Requirements

- All UCSD faculty, staff, and students listed as a PI or key personnel must complete appropriate CITI training
  - Biomedical Research and/or Social and Behavioral Research
  - IRB-Mandated course
  - Training refresher every 3 years
- If involved in NIH-funded research or pharmaceutical industry funded research, you must also complete CITI Good Clinical Practice training
  - Training refresher every 3 years

www.citiprogram.org
Study Start Up

- Site Qualification
  - Feasibility, Questionnaire, Survey, Visit, PI Credentials/Qualifications to conduct research

- Internal Review Processes
  - Does your division/department have a review committee?

- Budget Negotiations
  - Who will negotiate? Is budget feasible to continue with submission?

- Contract Submission
  - OCGA vs. OCTA

- Coverage Analysis?
  - Velos / EPIC Research Module
Study Start Up (continued)

- IRB Submission
  - Local or Central IRB
  - sIRB or Reliance pathway
- Ancillary Committees
  - Protocol Review and Monitoring Committee (PRMC)
  - Institutional Biosafety Committee (IBC)
  - Radiation Safety Committee (RSC)
  - COVID-19 Clinical Trials Review Committee
  - Embryonic Stem Cell Research Oversight (ESCRO)
  - Human Exposure Review Committee (HERC)
If you are conducting research at RCHSD, you must also submit a **Project Initiation Form** to Rady’s Research Administration ([research@rchsd.org](mailto:research@rchsd.org)).

Rady’s will issue Ready to Accrue and specific Rady’s #

- Final approval may require approval from medical directors, unit nursing, etc.
Regulatory Documents

- IRB Federal Wide Assurance Letter (see irb.ucsd.edu, General Guidance)
- IRB Application and Communications
  - Protocol
  - Investigator Brochure or Product/Device Information
  - Informed Consent/Assent/Parent Permission
  - California Experimental Subject’s Bill of Rights
  - UCSD or RCHSD HIPAA Authorization Form
  - Patient-Facing Study Materials (Questionnaires, Guides, Emergency Cards)
  - Recruitment Materials
  - FDA May Proceed Letter
- Blank CRFs
- Study Manuals
Regulatory Documents (continued)

- Logs
  - Monitoring Visit Log
  - Screening & Enrollment Log
  - Delegation of Authority Log
  - Temperature Logs
  - Protocol Deviation Log
  - Adverse Event Log
  - Concomitant Medication Log

- Essential Docs
  - FDA 1572 (Drug) or Investigator Statement (Device)
  - Protocol and Investigator Brochure Signature Pages
  - CVs and Medical Licenses
  - Conflict of Interest & Financial Disclosure Forms
  - Lab Certifications and Reference Ranges
  - Training Documents
Regulatory Documents (continued)

- Safety
  - Serious Adverse Events or UPRs
  - IND Safety Reports
  - Summary Safety Reports (6-month SUSAR line listings, Development Safety Update Reports)
- Equipment Calibration Records
- Subject Visit Tracking
- Sponsor Correspondence and Site Correspondence
- Monitor Reports
- Other
Reportable Events

- Violations, Adverse Events, UPRs, and Exceptions
- What constitutes a reportable event?
- What time frames apply?

- Reportable events may be identified by a PI, study team member, sponsor, or by internal audit
  - Both UCSD and RCHSD regularly conduct internal audits of research activity
# Food and Drug Administration: The Big Five Common Compliance Hurdles in Clinical Research

**UCSD Research and Compliance and Integrity, Office of Research Affairs**  
**Newsletter December 2019 | Volume 3, Issue 1**  
**Author: Jeffrey Simmons**

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<td>“Failure to obtain informed consent from study subjects”</td>
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| 2. Protocol Deviations & Violations | “Failure to inform the IRB of change to the protocol”  
“Failure to conduct your study in accordance with the approved protocol” | Changes made to the protocol without first notifying the sponsor & IRB                                                                 |
| 3. Drugs & Device Accountability | “Failure to maintain device accountability records”                                                | Inadequate record keeping related to investigational drugs & devices                                                                       |
| 4. Inadequate Medical Records   | “Failure to maintain adequate and accurate records”  
“Failure to maintain accurate, complete, and current subject records” | Trial related source documentation is not properly recorded which can lead to problems especially if the subject suffers an adverse event |
| 5. IRB approval not obtained    | “Failure to adhere to the general and specific responsibilities of a clinical investigator”        | IRB approval not obtained or lapse in IRB approval (no continuing review)                                                                       |
Policy:

“Federal regulations require that any modification to an approved protocol must be reviewed and approved by the IRB prior to implementing the change except when necessary to eliminate apparent immediate hazards/risks to subjects.”

- Negative impact on the rights, welfare, and safety of human subjects who participate in research.
- Research activities include all activities related to recruitment, consent, protection of privacy and confidentiality and all information outlined in the IRB reviewed and approved application/protocol.
“Investigators are required to conduct their research according to the plans reviewed and approved by the IRB. Instances where this does not occur, either inadvertently due to circumstances beyond the investigator’s control, or due to errors of omission or commission by research project staff, are considered violations and must be reported to the IRB in a timely fashion.”

*Even with the best of intentions any deviation from the protocol is a violation.*
Reporting Violations

- Major violations must be **reported to the IRB within 10 working days** of awareness of the violation.
  - The clock starts as soon as anyone on the study team is aware.
- “Major violations include instances that impact participant safety, substantially alter risks to participants, are non-compliant with applicable UCSD IRB, federal, state and institutional policies and regulations, or any instance determined by the IRB Chair, IRB Director or IRB Associate Director to require review by a convened IRB.”
- Deviations in eligibility are considered major violations. Eligibility criteria have been determined for to ensure both patient safety and data integrity.
Major Violations

- Any deviation without prior IRB review to eliminate apparent immediate hazard to a research subject
- An event or incident that results in an outcome that meets the criteria for an unanticipated problem involving risk to participants or others
  - Example: Blood drawn in excess of IRB-approved protocol resulting in hospitalization and blood transfusion
- A serious accidental or unintentional change to the IRB-approved protocol that alters the level of risk
  - Example: The investigator didn’t lower the dose in response to the subject’s weight change and the subject received a higher dose than the protocol allowed; increasing the subject’s risk of side effects
- Failure to obtain legally effective informed consent
  - Example 1: Consenting a non-English speaking patient with English consent.
  - Example 2: Using an adult consent for a pediatric patient instead of an assent with parent permission.
Major Violations Cont.

- **Study procedures that are done that are not approved by the IRB**
  - Example: A patient is asked to complete a research questionnaire without obtaining IRB approval first.

- **Incorrect research treatment** or intervention given to the subject
  - Example: the wrong dose or the wrong intervention is given

- **Failure to report** serious unanticipated problems/adverse events involving risks to subjects or others to the IRB

- **Failure to perform** a required lab test or perform a study visit/study labs during the required time frame, that, in the opinion of the PI, may affect subject safety or data integrity
  - Example: Missed triplicate ECGs after dosing as required by protocol.
Non-Compliance

- Serious noncompliance includes
  a) noncompliance that results in **substantive harm** or damage (or risk of substantive harm or damage) to the **safety**, **rights**, or **welfare** of human subjects, research staff, or others; or
  b) noncompliance that substantively **compromises the integrity or effectiveness** of the research.

The Committee determined that this report did disclose serious noncompliance in the matter of enrolling a subject without IRB approval and serious and continuing noncompliance for conduct of research procedures engaging an institution in human research without their own IRB approval in the matter of two subjects treated on-study at Kaiser.
Consequences

- UCSD IRB has the authority to **suspend or terminate investigators and/or protocols** that are found to be non-compliant with institutional policies and procedures, state laws, and/or federal laws or regulations or have been associated with unexpected serious harm to subjects.

- Notice will be made to the Vice Chancellor’s office in situations of continued non-compliance.
Sanctions that may be imposed by the IRB include, but are not limited to:

a) suspension or termination of project(s);

b) more frequent review of project(s);

c) compliance audits;

d) letters of censure;

e) restrictions on serving as an investigator on human subjects protocols;

f) research privilege probation;

g) suspension or termination of research privileges;

h) requiring additional education and training of the investigator or their research staff;

i) embargo or retraction of publications;

j) reporting of noncompliant activities to governmental entities (e.g. the Office of Human Research Protections (OHRP) and the US FDA);

k) or reclassification as possible scientific misconduct.
Kuali IRB Portal

Reportable Events

Report an Event

Event Type | Description | Status | Event Date | Recorded Date
--- | --- | --- | --- | ---
0 of 0 reportable events

Load 25 at a Time
Kuali IRB Reportable Event Categories

- Unanticipated Problem
- Protocol Deviation performed without prior IRB approval to eliminate an immediate hazard to a study participant
- Breach of Confidentiality
- Participant Complaint
- Hold, Suspension, or Early Termination of Research
- Noncompliance - possible Serious and/or Continuing Noncompliance
- Report(s) from Monitor, Sponsor, or Federal Agency
- Other
Staff Actions (Major Violation)

You suspect there may be a major deviation. What is next?

**Step 1.** Report potential major violations to your Principal Investigator (PI) as soon as possible. Major violations are to be reported within 10 days of knowledge of the event.

**TIP:** Always ask the PI and/or treating investigator if the violation placed the subject at risk, even if at theoretical risk.
Staff Actions (Major Violation) Cont.

**Step 2.** Work with the PI to report the violation to the IRB as appropriate. Include a narrative of the subject’s history, current study status, and description of the event/violation.

This is a formal report. Fully describe the event with an outside audience in mind. The reviewer will not have any previous history with the subject and will not access the research record for information. What information we provide is what will be reviewed.

Do not use shorthand, be clear and concise, spell out abbreviations, and include all pertinent details.

**Do NOT include patient identifiers in the report.**
Staff Actions (Major Violation) Cont.

The report should include:

- Subject study ID
- Date and description of event
- Description of the investigator's response (corrective action)
  
  Note – informing the patient/re-consent, updating the study documents, and reporting the violation are examples of the corrective action.

- PI’s assessment of the event or an evaluation of the risk to subject
- Any costs (if known) and who paid the costs (if known)
- Description of procedures will be done in the future to prevent a similar violation (preventative action).
  
  Note - retraining alone is not a sufficient preventative action. A change in the workflow to ensure the same error is not repeated is a more comprehensive preventative action.
Staff Actions (Major Violation) Cont.

Step 3. Implement appropriate corrective and preventative actions (CAPA) as reported to the IRB.

NOTE - A CAPA plan (change in the workflow) should not be discontinued or modified without written notice and prior approval from the IRB.
Adverse Events (AEs)

- Maintain an AE log that reports the event, dates of occurrence, response, and assessment of relatedness, causality and seriousness (grade).
  - Note - the individual tasked with assessing relatedness, causality, and seriousness should be medically qualified for that task.

- AEs are not reportable to UCSD IRB unless they are serious.
Some AEs may be Serious Adverse Events (SAEs).

- An event that results in death, hospitalization or prolongation of hospitalization, disability, or congenital abnormalities/birth defects.
- An event that is life-threatening or requires intervention to prevent permanent damage/disability.
- Other - refer to the protocol for study specific definitions or exclusions.

Report the SAE to the sponsor within 24 hours of knowledge of the event or per the reporting timeline as written in the protocol.

Report all SAEs to the IRB. Reporting dependent on UPR criteria.
Adverse Events vs. UPRs

- An AE or SAE maybe classified as an *Unexpected Problem Involving Risk (UPR)*. A problem or event, which in the opinion of the Principal Investigator was:
  - unanticipated,
  - serious, **AND**
  - at least possibly related to the research procedures.

An event **MUST** meet **all 3 criteria** to be classified as a UPR.

- UPRs are reportable to the IRB within 10 working days of the event.
  - The clock starts when anyone from the study team becomes aware of the event.
  - Failure to report major deviations are also reportable as deviations to IRB SOP.
UPRs - Unanticipated

- Unanticipated or unexpected
  - The event, problem, or risk is not mentioned in any study document including but not limited to protocol, investigator brochure, package insert, consent document, toxicity management guidelines, Safety Data Sheet (SDS), etc.
  - An unexpected severity of a known risk
    - Example: Grade 2 anemia expected, but Grade 4 anemia requiring hospitalization and blood transfusion is reported
  - An unexpected frequency of a known risk
    - Example: Headaches are expected in 20% of subjects but are being reported in 72% of subjects locally.
  - The event is also not contributable to the underlying disease.
UPRs - Serious or Involves Risk

- Serious
  - Did it place the patient or staff at risk for injury or greater injury? This is a medical judgment and should be provided by the investigator.
  - Did it meet the criteria for SAE?
    - Death or immediately life threatening
    - Threat of significant disability or injury
    - Requires hospitalization or prolongation of existing hospitalization
    - Congenital abnormality or birth defects
    - Is an important medical event that may jeopardize the patient or may require medical intervention to prevent 1 of the outcomes listed above.
UPRs - Related to Research

- At least possibly related to study procedures (not just study drug)
  - Investigator assessment of the event in their medical opinion

*Remain consistent in documentation (for example: AE log, sponsor SAE report, UPR, non-UPR, EPIC note, etc.)*
UPR Reporting

- Events meeting all 3 criteria for a UPR are to be reported to IRB within **10 working days** of the knowledge of the event by any research staff member; investigator and coordinator alike.

  In Kuali IRB you will use the Reportable Events tab.

- When a subject injury occurs that is at least possible related to study and medical costs are incurred (regardless if the event was anticipated or a UPR), the Investigator must notify the Clinical Research Billing (CRB).
UPR Reporting - CRB Notification

- UCSDHP Policy 342.2 - Clinical Research Billing
  - Subject Injury:

    Within 48 hours of the study team learning about a subject injury, the study team should notify CRB by sending an email to CRB@health.ucsd.edu requesting a bill hold for the charges for patient and the date(s) of service.

    Bills will remain on hold until the attribution of the subject injury has been determined.

    RCHSD has a separate process. Check with your study team lead.
Non-UPR & Minor Violations

- SAEs and minor violations are reportable to the IRB. A log format is suggested, but IRB has no current required format.
  - Log should include an assessment of attribution, relatedness, and expectedness.
- The log is reported at the time of the IRB renewal.

- If an SAE does not meet the criteria as a UPR, add it to the log.
- A deviation does not meet the definition of a major violation, add it to the log.
Staff Actions (UPR)

Step 1. An event or problem has been identified

Step 2. Assess seriousness, relatedness, and whether or not it was expected

Step 3. If it does not meet all 3 criteria for UPR, make entry in log for later submission.

Step 4. If it does qualify as a UPR; a reportable event submission should be drafted with sufficient information for an outside reviewer to have knowledge of the event and to assess the medical actions taken.

**Do NOT include patient identifiers in UPR report**
Deaths

- **Unexpected** subject **deaths at least possibly related** to study drug or study participation are immediately reportable to IRB **within 24 hours** of the research team's knowledge.

- Other potential reporting requirements:
  - Sponsor notification per protocol
  - FDA MedWatch report, if an investigator held FDA application
  - Data Safety Monitoring Board
  - Institutional Biosafety Committee if research is approved under a Biohazardous Use Authorization (BUA)
  - Clinical Research Billing for injury compensation review
COVID-19 Reporting

- Actions taken to mitigate or reduce risk due to COVID-19 for **existing** subjects are allowed without prior IRB approval but are still reportable.
  - Remote consent, TeleHealth Visits, missed appointments, use of outside labs
- They are minor protocol deviations and are reportable for tracking.
- Submit with annual renewal.

- If you foresee a continual or potential need for COVID-19 related actions, the recommendation is to incorporate them into your new study or amendment application ahead of time.
Breach in Confidentiality

- All UCSD consents should include Risk of Loss of Confidentiality in the risk discussion of the consent. It is therefore a known risk (i.e. not unexpected) and should be reported to the IRB as a minor deviation during the annual renewal.
  - Example: Page 2 of the lab report was sent to a sponsor with the subject's name unredacted.

- Breach in confidentiality with a more severe or greater consequence may be submitted as a reportable event.
  - Example: Unauthorized disclosure of the sensitive health status of a subject like HIV screening results.
Breach in Confidentiality Cont.

- Policy UCSDHP 4: Any breach in confidentiality is required to be reported to The Office of Compliance and Privacy.
  
  - Reporting is an institutional requirement and is not dependent on research vs. standard of care, seriousness, relatedness, or expectedness.

- Health System reporting:
  
  - iReport online (category: confidentiality)
  - calling Privacy Office (858-657-7487)
  - e-mailing hscomply@health.ucsd.edu.

- Campus reporting: ucsdprivacy@ucsd.edu (Campus Privacy Office)

- The primary contact, the person with the most information on the event, should act as the reporter.

- Report as soon as possible - same business day preferred.
Protocol Exception to Enroll an Individual Subject

Definition: Allowance of a one-time enrollment of a single individual who does not meet the inclusion/exclusion criteria of an approved protocol.

Protocol Exception to Enroll requests should be rare and clearly determined to be in the best interest of the patient.

The subject may not be enrolled until approval has been granted from a full board IRB.

If screening procedures are in progress at the time the patient’s ineligibility is determined, all future research procedures must cease until such time the IRB approves for the continuation and grants an eligibility waiver.
Staff Action (Exception)

Process for Requesting an Exception:
Work with your PI to draft a request to the IRB as an amendment. Do not include patient identifiers in this request.

1. Documentation of approval by the study sponsor to provide the exception, as appropriate.

   *Written approval from sponsor must be obtained prior to IRB submission. Not all sponsors accept eligibility waivers.*

   *Provide this documentation. Documentation could include e-mail correspondence, sponsor waiver form, or medical monitor review form.*
2. Clarify if the protocol’s inclusion/exclusion criteria will be updated with a future amendment.
   - If yes, the timeframe for submitting the amendment to the IRB.
   - If no, justification for not submitting such an amendment including why modifying the inclusion/exclusion criteria are appropriate for this subject and not all potential subjects.

3. Clarify if data collected on this subject will be provided to the study sponsor or be included in the data analysis for the study.
Staff Action (Exception) Cont.

4. Why it is appropriate to enroll this subject is this protocol.

5. What specific study criteria are not satisfied by the subject?
   Quote the specific eligibility criteria not met and provide patient narrative including the reason for the patient not meeting criteria.

6. Justification of potential risk to the subject.

7. Have other protocol exception(s) been done on this study. If so, provide a brief description of each.
   Regulatory will provide a summary of known previous exceptions.
Corrective and Preventative Action Plan (CAPA)

- A CAPA should address the corrective actions addressing the immediate event and a preventative action should address how the event will be avoided in the future.
- A good CAPA will examine and address the root cause.
- Re-training alone is not a sufficient preventative action. Consider change in the workflow such as a second reviewer or additional source document.
- Ensure your CAPA is feasible. You do not want to promise a plan you are not able to comply with long term.
- Depending on the event, consider employing the CAPA across in all of your research projects and not just the single project. Look at bettering your program as a whole.
- Maintain documentation of CAPA compliance.
The subject was to have a PET scan using an experimental radioactive tracer, rather than the approved tracer for PET scans. Due to the vials of experimental tracer looking similar to the approved tracer, the subject was given the wrong tracer to initiate the exam.

The error was discovered before the entire dose of tracer was given and the procedure was stopped. Dr. Smith, a sub-investigator and attending radiologist for the study was immediately informed of the error. The sponsor was contacted the same day regarding the mistake before proceeding further with the study.

The sponsor allowed the scan to proceed using the wrong tracer. Dr. Smith felt that this did not present a safety risk to the subject.

The patient was informed of the situation and was also in agreement with continuing.

The dose of tracer was given and the scan proceeded without further incident.
Choose the best corrective and preventative action plan:

A. Submit an Unexpected Problem involving Risk report and continue to observe the patient for side effects. Call for a full review of the protocol and review of the radiation program. Discontinue the use of that manufacturer of the tracer.

B. Notify the IRB of the deviation and re-train the staff to look more closely at the vials before administering the tracer the next time.

C. The patient wasn’t harmed due to the mix up and the sponsor allowed the research to continue, so no follow-up is required. It won’t happen again.

D. Notify the IRB and Radiation Safety of the deviation. Request the manufacturer to change the packaging of the vials to better differentiate the tracers. Create a secondary check by another research staff member to verify use of the correct tracer prior to administration and document the verification. Re-train the staff on the use of the new vials and dual verification process.
A. Close but not quite right! Notifying the IRB is an acceptable corrective action but discontinuing the tracer manufacturer before you have requested revisions from them is extreme and may prevent the research from moving forward.

B. Incorrect! Re-training alone is not a comprehensive preventative action. A change in the workflow in addition to re-training would be a better response.

C. Incorrect! Even though the patient was unharmed there was the possibility of harm and a risk of the error occurring again. This event was unexpected, related to the research, and involved potential increase in risk to the subject.

D. Correct! The event meet all of the criteria for reporting to IRB and because this involved a radioactive investigational agent, Radiation Safety was also notified. The CAPA included a plan that addressed the root cause on multiple levels: re-labeling the vials, revising the workflow, and re-training.
The goal is to have the most **complete, accurate, and reliable** data possible. A good standard to follow is ALCOA-C.

- **Attributable**
  - Traceable to person, date, visit
  - Initial/sign and date all written entries
  - If you line through something, initial and date the correction
  - All entries, corrections, and alterations should be made by personnel on the study DOA

- **Legible**
  - Recorded in a permanent medium (ink or unalterable electronic records)
  - Original entry must be readable
    - No blacking out, whiting out, or redacting (except when necessary to comply with HIPAA)
ALCOA-C Cont.

- **Contemporaneous**
  - Documented in real time? Don't back date.
  - If entering data at later date that originally captured, *initial and date* with current date and write "late entry"
  - Date must be completed at the time of signature by same person signing the form (no pre-dating)

- **Original**
  - Hard copy, or if electronic, is there an audit trail?
  - Original records should be retained at the study site

- **Accurate**
  - Unaltered and correct
  - Corrections- single line through with initials and date

- **Complete**

Think like an auditor! Would the documentation be clear to a 3rd party?
OIA SOPP 3.14 - Protected Populations

“In studies where subjects likely to be vulnerable to coercion or undue influence are likely to participate, appropriate additional safeguards must be included in the study to protect their rights and welfare.”

Involvement of protected populations (aka vulnerable subjects) requires full committee review and approval before being allowed to move forward.
Vulnerable Subjects

- Includes:
  - Surrogate Consent and Cognitively Impaired Persons
  - Children and Adolescents
  - Prisoners
  - Pregnant Women and Fetuses or Fetal Tissue
  - Students and Employees
  - Economically disadvantaged
Decisional Capacity & Ongoing Consent

- Whenever possible, investigators will attempt to obtain informed consent directly from the subject.
- IRB application provides a protocol-specific plan for the sequence of steps that will be employed to acquire and document surrogate consent provided by a legally authorized representative.
- These types of requests or amendments will always be considered major amendments and require full review by a convened IRB committee.
- Informed consent is a continual process. If your subject loses the ability to make decisions for themselves, the patient must be evaluated for the ability to make an informed decision.
Surrogate Consent (non-emergency)

- If subject is **clearly lacking** decision-making capacity:
  - Document the observations and clearly state the factors of the assessment.
  - Determine appropriate surrogate.
- If subject has **questionable** decision-making capacity:
  - Describe the research to the subject.
  - Use a standardized process to assess and document the subject’s decisional-capacity. Be consistent with the plan as documented in the IRB application!
  - Inform the subject of the intent to use a surrogate consent. Any dissention, objection, or resistant from the subject will result in aborting their participation.
  - Document subject’s willingness and record the discussion with both the subject and their surrogate consenter.
Surrogate consent may be obtained from any of the following potential surrogates who has reasonable knowledge of the subject, in the following descending order of priority:

1. The person’s agent designated by an advance health care directive.
2. The conservator or guardian of the person having the authority to make health care decisions for the person.
3. The spouse of the person.
4. The domestic partner of the person as defined in Section 297 of the Family Code.
5. An adult son or daughter of the person.
6. A custodial parent of the person.
7. Any adult brother or sister of the person.
8. Any adult grandchild of the person.
9. An available adult relative with the closest degree of kinship to the person.
Perform decisional capacity assessment as outlined in research protocol and approved by IRB.
Knowledge Check

There is an adult patient sedated and intubated in the ICU and the investigator wishes to enroll them on to their research project. The patient's condition is not life threatening and their mother is present and in communication with the medical team concerning their care. The patient has an advance directive on file. Can the patient participate in the research through a surrogate consent?

A. No, the investigator must first wait until she is conscious and ask if she agrees with the surrogate consent.
B. Yes, with the IRB's approval for using surrogate consent and the advance directive indicating their mother as their agent.
C. No, they must wait until the patient's spouse arrives to make the decision.
D. Yes, she won't know what's happening anyways, so the investigator can proceed.
Knowledge Check - Confirmed

A. Incorrect! If the patient is clearly not of decisional capacity, the investigator should document their observation and proceed with identifying the appropriate surrogate.

B. Correct! Use of surrogate consent must be approved on a non-emergent basis by the IRB prior to initiating the consent. Individuals named as the patient’s agent in an advance directive are the priority for serving as a surrogate.

C. Incorrect! If the mother is the patient’s surrogate as named in the advance directive, the spouse does not act as the surrogate although the family may need to discuss it together before proceeding.

D. Incorrect! The patient cannot decide for themselves but their rights as a human subject are protected!

Respect for Persons - Individuals should be treated as autonomous agents, and persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.
Sigh...

So what I hear you saying is you'll pay me to get cured—I'm in!!
Resources

- UCSD Office of IRB Administration (OIA)
  - Website: irb.ucsd.edu
  - Main Office Phone: (858) 246-4777
  - E-mail: irb@ucsd.edu

- The Office of Compliance and Privacy
  - Helpline for research / clinical trial related issues (858) 657-7487 or hscomply@health.ucsd.edu
  - Website: https://pulse.ucsd.edu/departments/compliance-advisory-services/Pages/default.aspx

- Research Compass (ACTRI site)
  - compass.ucsd.edu
RCI COMMUNICATIONS

- Research Compliance and Integrity Helpline: (858) 822-4939, rci@ucsd.edu
- RCI Office Hours, Tuesdays from 11-12: https://calendly.com/ucsdrcioffice
- Conflict of Interest Helpline: (858) 534-6465, info-coi@ucsd.edu
- Export Control Helpline: (858) 246-3300, export@ucsd.edu
- IACUC Helpline: (858) 534-6069, iacuc@ucsd.edu
- Unannounced Governmental and Law Enforcement Hotline: (858) 246-4600
- Hot Topics Eblasts and Newsletters: http://blink.ucsd.edu/sponsor/rci/news.html

- RCI Hot Topics Training Program: https://blink.ucsd.edu/sponsor/rci/research-compliance-hot-topics.html
- To be added to the RCI list serv, please email rci@ucsd.edu