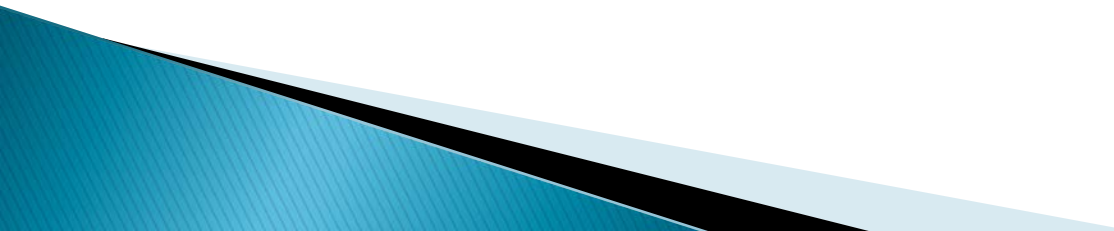


# Clinical Research Billing Compliance

University of California, Compliance & Audit Education Series:  
*“Clinical and Human Subjects Research: Monitoring Your Compliance Program”*  
June 23, 2015



# Agenda

1. Clinical Research Billing Compliance Risks
  2. Benefits of a CRB Compliance Program
  3. Implementation of a CRB Compliance Program
  4. What is a “Qualified” protocol billable to insurance?
  5. What Are the CRB Special Billing Rules?
    - **Challenges**
    - **Resources to implement the CRB Program**
    - **Auditing the Clinical Research Billing Program**
- 

# Clinical Research Billing Compliance Risks

## Billing for services that are:

1. Not covered under the Medicare Clinical Trial Policy and/or other Medicare rules. Not a Medicare Covered Service
2. Experimental procedures not covered by commercial payers
3. Paid by Sponsor (Double billing)
4. Promised free in the Informed Consent
5. Not accurately reported as required on the billing claim  
(special billing rules, device, procedure codes, units, etc.)
6. Not supported by required documentation  
(documentation of medical necessity and study participation)



# Benefits of the CRB Compliance Program

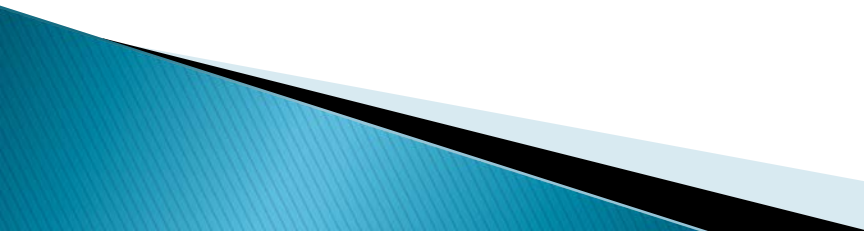
- Support Organizational Mission/Vision
- Reduce/Mitigate risks of noncompliance
- Reduce potential for enforcement actions
- Support research program integrity

# The CRB Compliance Program

## The Implementation Plan:

- ▶ Commitment to develop Coverage Analysis (CA) for all clinical research studies which could generate charges in either the hospital or physician billing systems;
- ▶ SOPs describing process and assurance mechanisms for synchronizing the research informed consent, clinical trial agreement/budget and Coverage Analysis for new studies;
- ▶ Timeline for roll-out of Coverage Analysis for new studies and all legacy studies (those active with enrollees that receive services which could generate charges);
- ▶ A database of clinical research studies which have active enrollment or are open to enrollment (the database shall indicate whether a Coverage Analysis exists);
- ▶ Process for the health sciences campus to implement a CTMS or database;
- ▶ Process on how research teams will update database with MRNs of enrolled subjects;
- ▶ Document housing plan which allows central storage of study documents and the CA;
- ▶ Description of how hospital and physician billing offices and research compliance can access the CA, subject enrollment database, and study documents; and
- ▶ Identification of individuals in operations who are responsible and accountable for managing the coordination of information for CRB and have the authority to coordinate resolution of CRB errors ■

# Implementation of a CRB Program

- ▶ Hire/train the right people who have the skills/expertise (qualifications) for the CRB procedures.
  - ▶ Develop standards for processes, procedures including outcomes/results
  - ▶ Ensure adequate and complete documentation for all procedures and results (e.g. written SOPs)
  - ▶ Provide training programs for completing Coverage Analysis, implementation of a CTMS, reviewing billing claims...
  - ▶ Collect, track and measure metrics on the results/outcomes of the procedures and billing
  - ▶ Perform periodic Quality Assurance Measurements to ensure conformance to procedures
  - ▶ Implement CAPA actions to improve quality and performance
- 

# The CRB Compliance Program

## Operational CRB Policies, Procedures, Regulations

- **Ensure internal policies comport with UC Policy/Guidance, governing Laws/Regulations**
- 21 CFR 50.25 (b)(3): FDA Regulation on Human Subjects, Informed Consent
- 42 CFR 405 Federal Health Insurance for the Aged and Disabled, § 203 FDA categorization of investigational devices
- 45 CFR 46.116(b) (3): Department of Health and Human Services (DHHS) Regulations on the Protection of Human Research Subjects
- American Medical Association (AMA) Code of Procedural Terminology (CPT)
- American Medical Association (AMA) Evaluation and Management Services Documentation Guidelines
- California Senate Bill No. 37, 2001. Health insurance: coverage for clinical trials
- Centers for Medicare and Medicaid Services (CMS) Medicare Claims Processing Manual, Pub 100-4; Chapter 32, § 69.6 (Billing for Clinical Trials)
- Centers for Medicare and Medicaid Services (CMS) Medicare National Coverage Determination for Clinical Trials 310.1
- Centers for Medicare and Medicaid Services (CMS) National Correct Coding Initiative Edits (NCCI Edits - Physicians)
- False Claims Act, 31 U.S.C. 3729
- Federal Register 65-Office of Inspector General (OIG) Compliance Program Guidance for Third Party Medical Billing companies, Hospitals, Individual and small group Physician Practices
- Federal Register 68, Office of Inspector General (OIG) Compliance Program for Pharmaceutical Manufacturers
- Office of Inspector General; Office of Management and Budget Circular A-100, A-21
- Patient Protection and Affordable Care Act (PPACA), HR 3590, § 2709. Coverage for Individuals Participating in Approved Clinical Trials

**Stay current – Subscribe to CMS and local MAC email updates**

**Review Private Payer Coverage Requirements**

# Challenges with Implementation

## Communication across the Enterprise

- ▶ Leadership Messaging to authorize, require, and direct participation
- ▶ Research System(s) Build and Training
- ▶ Hospital billing ↔ Professional billing ↔ Study Team ↔ EMR/IT
  - ▶ Research study corrections
  - ▶ Scheduling Issues
  - ▶ Post-service charge corrections – define and implement your process
  - ▶ Refunds and corrected claims
- ▶ Completing an accurate Coverage Analysis
- ▶ Subject Protocol Visit Dates
- ▶ Study Fund Account Issues
- ▶ Research Rates and Research Charge master. Set-up for Federal, Pharma, cash rates



# What Is An “Approved” Study?

1. Will the trial evaluate an item or service that falls within a Medicare benefit category and not statutorily excluded from coverage?

2. Does the trial have therapeutic intent, i.e.. not designed exclusively to test the toxicity or disease pathophysiology?

3. Will the trial enroll patients with the diagnosed disease, i.e.. not a Phase I study enrolling only healthy volunteers?

1. Is the trial funded by NIH, CDC, AHRQ, CMS, DOD or VA?

2. Is the trial supported by centers or cooperative groups that are funded by the NIH, CDC, AHRQ, CMS, DOD or VA?

3. Is the trial being conducted under an Investigational New Drug application (IND) reviewed by the FDA?

4. Is the trial a drug trial that is exempt from having an IND under 21 CFR 312.2(b)(1)? (see Appendix A for exempt drug trials)

# What Is An “Approved” Study? (cont.)

1. Is the purpose of the trial to test whether the intervention potentially improves the participants' health outcomes?
2. Is the trial well-supported by available scientific and medical information or intended to clarify or establish the health outcomes of interventions already in common clinical use?
3. Does the study NOT unjustifiably duplicate existing studies?
4. Is the trial designed to answer the research question being asked?
5. Is the trial sponsored by a credible organization or individual capable of executing the proposed trial successfully?
6. Is the trial in compliance with the Federal regulations relating to the protection of human subjects?
7. Will all aspects of the trial be conducted according to the appropriate standards of scientific integrity?

# Audit Readiness

Studies with billing risks are reviewed to verify if trial is a “**qualified clinical trial**”.

The compliance auditor will review the **clinical trial agreement**:

- Confirm that all items/services that are billable to the sponsor/research account per the contract are on the coverage analysis according to the timeline in the trial.
- Review contract for subject injury and adverse event payment and match it with the cost language in the consent.
- Identify the services the sponsor is paying for and verify that the coverage analysis does not show we are billing a third party payer for those services.

The compliance auditor will review the **informed consent**:

- Verify that the informed consent addresses patient financial responsibility and specifies items/services covered by the research and the sponsor
- The cost language for adverse events and subject injury is matched to the clinical trial agreement.

# Audit Readiness (cont.)

- ▶ The compliance auditor will review the **Coverage Analysis** to:
  - Identify the correct payer is documented in the coverage analysis
  - Review study procedure section and schema in the protocol to compare items/services required by the protocol and those listed on the coverage analysis, not just those items listed in the study calendar
  - Note any discrepancies that may generate a charge
  - Verify that the designations of items/services in the coverage analysis are accurate and include supporting comments in the CTMS or other electronic database
  - Verify that all HCPCS and CPT codes are correct
  - Verify that HCPCS and CPT codes are appropriately identified as routine costs in a qualified clinical trial or should be billed to study
  - Verify ClinicalTrials.Gov registration number appears in system
  - Confirm that the coverage analysis is consistent with the protocol, the informed consent, and the clinical trial agreement
  - If the trial is a device trial, verify that CMS/Noridian has been notified of study and IDE approval letter is uploaded into the CTMS/database
  - Completed coverage analysis in CTMS/database can be used for patient level billing and invoicing
  - There are no billable items for services that are for research purposes only.

# What Are the CRB Special Billing Rules?



## NCT#

- Registration Number issued upon study registration with ClinicalTrials.gov
- Required on claims for items/services provided as part of a CMS approved study or Registry

## V70.7 Diagnosis Code –“examination of participant in clinical trial”

- Reason for the experimental or investigational service should be first-listed diagnosis.
- **ICD-10 code change: Z00.6** – Encounter for examination of normal comparison and control in clinical research program.

## Condition Code 30

- “qualified clinical trial”
- must appear on the hospital claim for items/services related to a Qualified Clinical Trial regardless of whether all services are related to the clinical trial or not.

## Q0 and Q1 Modifiers

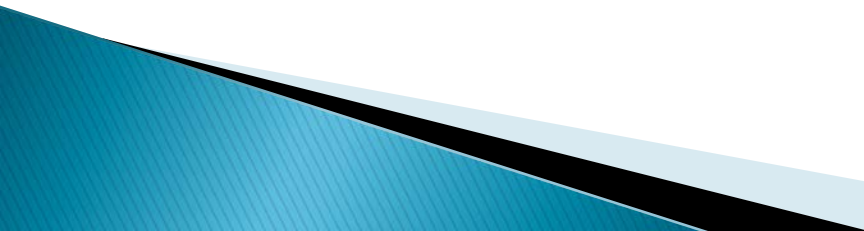
- used on the billing claim form to characterize the line-item service as investigational or a routine cost in a Qualified Clinical Trial.
  - Q0 – investigational (object of the trial) drug, device or procedure
  - Q1 – routine

## Investigational Device Codes and Modifiers

- 624 – investigational device revenue code reported with IDE number
- FB modifier and assign nominal charge – designates item was provided at no cost

# Audit Readiness – Record Production

Keep the following information/documents readily available for production to internal and external auditors:

1. IRB Approved Study Protocol and Informed Consent (all versions)
  2. Clinical Study Agreement/Award and Budget (with amendments)
  3. Certified Coverage Analysis and supporting documents
  4. FDA Status Documents (IDE/IND Approval Letters)
  5. Pertinent Subject Medical Records and Signed Informed Consent
  6. Enrollment and protocol visit dates for each subject
  7. Study Invoicing/Payment Records
  8. Study Fund Account Transaction Records
  9. Any other relevant documents (e.g. Investigator's Brochure, Regulatory records)
- 

# Staying Current

## **CMS Clinical Trial Policy**

<http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=1&ncdver=2&bc=BAABAAAAAAAA&>

## **Medicare Managed Care Manual, Ch. 8**

<https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/mc86c08.pdf>

## **Medicare Benefit Policy Manual, Ch. 14 - Medical Devices**

<https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/bp102c14.pdf>

## **Medicare Claims Processing Manual, Ch. 32- Billing Requirements for Special Services**

<http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104c32.pdf>

## **Medicare Coverage Related to Investigational Device Exemption (IDE) Studies**

<http://www.cms.gov/Medicare/Coverage/IDE/>

## **CMS Coverage with Evidence Development**

<http://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html>

## **MM8401 Revised re Reporting of 8-Digit NCT# and billing requirements for institutional and professional claims for services provided under a clinical trial, clinical study, or registry**

<http://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/SE1344.pdf>

## **Clinicaltrials.gov**

<http://www.clinicaltrials.gov/>

## **CMS Email Update Subscriber**

<https://public-dc2.govdelivery.com/accounts/USCMS/subscriber/new?preferences=true>

## **OIG Work Plans**

<http://oig.hhs.gov/reports-and-publications/workplan/index.asp#current>

## **HHS Email Subscriber**

<https://public.govdelivery.com/accounts/USHHS/subscriber/new?preferences=true>

## **FDA Email Updates Subscriber**

[https://service.govdelivery.com/accounts/USFDA/subscriber/new?topic\\_id=USFDA\\_51](https://service.govdelivery.com/accounts/USFDA/subscriber/new?topic_id=USFDA_51)







**UC DAVIS**  
**HEALTH SYSTEM**

## Research Compliance: The Research/Privacy Nexus

*Shara Reed, JD MPH  
Deputy Compliance Officer*

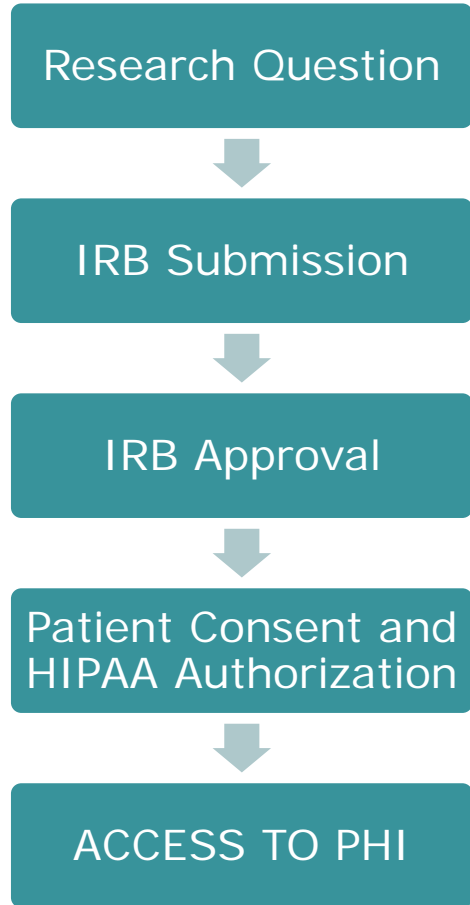
- De-centralized approach to research compliance with oversight provided from several areas including: IRB, CTSC, Office of Research, UCDMC Compliance Department
- UCDMC Compliance Department Role:
  - Training and Education
  - Staff Resource
  - IRB/CTSC/Campus “Linkage”
  - Involvement in Investigations
  - Routine audit/review activities related to:
    - Clinical Research Billing
    - Coverage Analyses
    - Tracking of Research Activities in EMR
    - Privacy

# Compliance Review: Research Privacy

- Primary Goal: Ensure compliance with state and federal privacy laws
- Focus:
  - What is the purpose of the access?
  - Is access authorized?
  - Is the access properly tracked/documentated?

- Access to Patient Records with Authorization
- The Rule permits covered entities to use and disclose protected health information (PHI) without authorization for treatment, payment and health care operations
- There are some exceptions for researchers:
  - (1) Waiver of HIPAA Authorization
  - (2) For Preparatory to Research purposes
  - (3) For Research on PHI of Decedents
  - (4) Limited Data Sets with a Data Use Agreement

# Access with Authorization



IRB Approval Number \_\_\_\_\_

University of California

Permission to Use Personal Health Information for Research

Study Title (or IRB Approval Number if study title may breach subject's privacy):  
\_\_\_\_\_

Sponsor/Funding Agency (if funded):  
\_\_\_\_\_

**A. What is the purpose of this form?**

State and federal privacy laws protect the use and release of your health information. Under these laws, the University of California or your health care provider cannot release your health information to the research team unless you give your permission. The research team includes the researchers and people hired by the University or the sponsor to do the research. If you decide to give your permission and to participate in the study, you must sign this form as well as the Consent Form. This form describes the different ways that the researcher, research team and research sponsor may use your health information for the research study. The research team will use and protect your information as described in the attached Consent Form. However, once your health information is released it may not be protected by the privacy laws and might be shared with others. If you have questions, ask a member of the research team.

**B. What Personal Health Information will be released?**

If you give your permission and sign this form, you are allowing your health care provider to release the following medical records containing your Personal Health Information. Your Personal Health Information includes health information in your medical records and information that can identify you. For example, Personal Health Information may include your name, address, phone number or social security number.

- |  |  |   |
|--|--|---|
| <input type="checkbox"/> Entire Medical Record | <input type="checkbox"/> Emergency Medicine Center Reports | <input type="checkbox"/> Outpatient Clinic Records      |
| <input type="checkbox"/> Radiology Reports     | <input type="checkbox"/> Progress Notes                    | <input type="checkbox"/> EKG                            |
| <input type="checkbox"/> Pathology Reports     | <input type="checkbox"/> History & Physical Exams          | <input type="checkbox"/> Radiology images               |
| <input type="checkbox"/> Laboratory Reports    | <input type="checkbox"/> Discharge Summary                 | <input type="checkbox"/> Psychological Tests            |
| <input type="checkbox"/> Dental Records        | <input type="checkbox"/> Consultations                     | <input type="checkbox"/> Health Care Billing Statements |
| <input type="checkbox"/> Operative Reports     |  |   |

Other: \_\_\_\_\_

# Review of Authorized Access for Research

- The Privacy Components of Research Audits:
  - Are HIPAA Authorizations signed by all enrolled patients?
  - Are HIPAA Authorizations properly completed?
  - Are HIPAA Authorizations properly filed in the record?
- These inquiries are made by both UCDCM Compliance and Office of Research Staff during routine audits
- Non-compliance reported to IRB and Compliance for follow-up, reporting and tracking



## Preparatory to Research Application

Resize font:



Please complete the survey below.

Thank you!

**This application should be used if you want to look at protected health information (PHI) for research purposes, such as evaluating whether a research project is feasible or not, identifying prospective research participants for the purposes of study development or to design data collection forms, etc., You do not need this form to access de-identified data through Cohort Discovery. We strongly encourage you to use de-identified data by seeking access through Cohort Discovery first. If you submit a preparatory to research application and we approve, the following rules apply:**

- 1. You must attest that the work is solely to review PHI to prepare a research protocol or for similar purposes preparatory to research.**
- 2. You must provide a statement affirming that no PHI will be removed from the covered entity by the researcher in the course of your review**
- 3. Provide a list of the requested information that meets the minimum necessary data to accomplish the goals of the research.**

**The UC DHS Privacy Board must approve the request. Please fill out the form below. You may be contacted for more information, if necessary.**

# Preparatory Research Requests

- What do you need the data for?
- What information do you need to review?
- Whose PHI do you want to see?
- What is the desired data source
- Have you considered cohort discovery?

If my application is approved, by checking the box, I affirm that the following statements are true:

1. The request to access PHI is solely to review as necessary to prepare a research protocol or for similar purposes preparatory to research
2. No PHI will be removed from the electronic medical record
3. The PHI for which use or access is sought is necessary for the research purpose
4. No potential research subject will be contacted as part of the preparatory to research

\* must provide value

I Agree  I Do Not Agree

reset

Submit



# Review of Preparatory Requests

- Primary Inquiries
  - Were records accessed appropriate?
  - Was information accessed appropriate?
  - Was access within time frame?
  - Did investigator comply with Accounting of Disclosures policy?
- Review undertaken by Compliance

## Accounting of Disclosures

- The Privacy Rule requires covered entities (UCDHS) to maintain records of certain disclosures without authorization, including disclosures to researchers (not part of the covered entity) including disclosures pursuant to a waiver of authorization, preparatory to research reviews, and decedent research (45 CFR 164.528)
- Under HIPAA, subjects can request a record of releases during six (6) year period

# Accounting of Disclosures – UCDHS P&P 2446

- Investigators who receive (view/disclose) protected health information (PHI) of the CE without a patient's written authorization are responsible for accounting for this access
- There are two ways to track disclosures:
  - Online Database
  - Quick Disclosure Activity in EMR/EPIC

# Accounting for Disclosures

**Access the Quick Disclosure**

1. Go to Hospital Chart or Chart
2. Click "More Activities and choose Quick Disclosure
3. Quick Disclosure opens. Fill out the appropriate fields
  - Purpose Field - type "Research" and choose the appropriate purpose
  - Info Requested - click the magnifying glass to see all categories
  - Authorization Received- click "Third Party" and type "UCD" in requester field then press enter.
  - Authorization Received? - choose "Yes" or "No"

**Category Select**

Title	Number
Amplulatory Clinic Records	565
Consultation Report	532
Demographics	592
Dental Records	593
Discharge Summary	140
Emergency Department Records	632
Entire Medical Record	573
Financial Records	594
History & Physicals	576
Imaging Reports	536
Lab & Pathology Reports	595
Mental Health Records	290
Operation reports	348
Outside Test Reports	591
Progress Notes	563
15 categories loaded	

## HIPAA Tracking of Disclosure

Please submit any questions to:  
 Joshua Simon [joshua.Simon@ucmc.ucdavis.edu](mailto:joshua.Simon@ucmc.ucdavis.edu) (916) 734-8959  
 Joe Golzro [joe.golzro@ucmc.ucdavis.edu](mailto:joe.golzro@ucmc.ucdavis.edu) (916) 948-6802

The Health Insurance Portability and Accountability Act (HIPAA) regulations require certain disclosures of patient health information to be tracked and reported to the patient upon request. Any patient or patient representative must fill out a [Request for Accounting of Disclosures Form](#), and submit the form to the Health Information Management Department at (916) 734-2126. All UCCHS workforce including but not limited to HBC, PCI, and IP services is responsible for entering the disclosed information in this database in a timely and accurate manner. For a quick overview, tips and tricks on UCCHS policy and procedure about HIPAA Tracking and Disclosing please go to [HIPAA Tracking and Disclosing Training](#). For any questions regarding the process please contact Health Information Management Department at (916) 734-6206.

Disclosures made for the following purposes **DO NOT** need to be entered:

- Routine disclosures for treatment, payment or health care operations (TPO).
- Disclosures to the individual (patient) such as appointment reminders, treatment alternatives, health-related benefits and services.
- Limited Data Sets and Hospital Outcomes.
- Individuals involved in patient care or payment of care.
- Disaster relief efforts.
- National security and intelligence activities.
- Correctional institutions (prisons).
- Incident Disclosures.
- Workers Compensation payment and/or patient care.
- Disclosures prior to April 14, 2003.

Patient Information	
MR Number	<input type="text"/>
First Name	<input type="text"/>
Last Name	<input type="text"/>
Birth Date	<input type="text"/> mm/dd/yyyy
Gender	- Select Gender -
Disclosure Date	<input type="text"/> mm/dd/yyyy
Recipient Information - Select Recipient -	
Name/Organization	<input type="text"/>
Address	<input type="text"/>
City	<input type="text"/>
State	<input type="text"/>

# The Surveillance Program: Research Activity

- The Surveillance Program is a proactive process for reviewing user access to records in systems of patient records (e.g., EMR)
- Cases are routed to our office where user access (typically PI or CRC) are to patient records without a discernable work purpose
- Primary Question: Is the access appropriate?

# Surveillance Program: Review of Research Cases

- Review Process for Surveillance Case:
  - Who is the user?
    - Review of protocol and RPL lists
  - Was IRB approval sought?
    - If yes, was Waiver provided?
    - If not, was another exception applicable (e.g., preparatory)
  - If HIPAA Authorization was required, was it obtained and included in the record?
  - If this is an Exception Case, was the Accounting of Disclosures policy followed and properly tracked?

# Outcomes of Research Privacy Reviews

- Educate, educate, educate
  - Policies and Procedures: accounting of disclosures, documenting in record, updating RPLs, etc.
- Process Improvements
  - Accounting of Disclosures
  - Encouragement of cohort discovery
  - Minimum Necessary Standards
  - Proper use of PHI for research purposes



# Thank you!

Shara Merritt Reed

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# Auditing Human Subject Research Protocols

Andrew Walton, Research Compliance Officer  
University of California, Compliance & Audit Education Series  
June 23, 2015



**UC Irvine Health**

# Why Audit Human Subjects Research Protocols?

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- *Safety of subjects*
- *HIPAA and Privacy concerns/protection of PHI*
- *Quality of the research & data Integrity*
- *Educational*
- *Provides opportunities for improvement and training*
- *Compliance with Federal and State regulations and guidelines*

# Research Compliance Office Audit Staff

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- *Research Compliance Officer*
- *Compliance Office Regulatory Specialist*
- *Collaborate with IRB and Internal Audit staff – joint audits and investigations*
- *Utilize Medical Center and Campus staff to facilitate audits*

# Routine Audits – Human Subjects Research

- *Review annually 5-10% of all treatment protocols*
- *Review protocols of new investigators*
- *Review new protocols prior to initiation*
- *Review every investigator every 2-3 years*



# For-Cause Audits – Human Subjects Research

- ***Whistleblower***
- ***Complaints***
- ***FDA Investigation***
- ***Facility policy not being followed***
- ***Protocols under current review of the IRB***
- ***Adverse Events***

# Preparation Prior to Auditing

---

The auditor will:

- *Read and understand the protocol/narrative*
- *Read IRB approved Research Consent and HIPAA Authorization*
- *Read IRB approval letters*
- *Review the Clinical Trial Agreement (CTA)*
- *Review IND and/or IDE Documentation*
- *If applicable, review the Coverage Analysis*

# Initiating the Audit

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# Initiating the Audit-Letter to Investigator

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**TO:** Name of Principal Investigator  
Academic Appointment Title  
Department  
Division, as necessary

**FROM:** Andrew Walton  
Research Compliance Officer

**RE:** *Research Protocol Audit*

As part of the continuing effort by the School of Medicine (SOM) to ensure the safety of participants enrolled onto human subject research protocols, the Office of Research Oversight conducts ongoing reviews of open research protocols. Protocols are generally selected when the Principal Investigator has not previously been audited or by the length of time since the last audit. It is a SOM goal to audit the Principal Investigator protocols approximately every 2-3 years. Our records show XXX (your last protocol audit occurred on **DATE**).

Please contact **NAME**, Regulatory Specialist, at extension XXXX within the next 5 days to schedule the audit. *Although you do not need to be present during the audit*, access to the files and documents selected for audit must be available to XX. In order to help you prepare for the audit, the following protocols were selected for examination:

**IRB NUMBER AND TITLE**  
**IRB NUMBER AND TITLE**



# Initiating the Audit-Letter to the Investigator

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## Source documents required for the audit include:

- Master Protocol
- Investigator's Brochure, as applicable
- IRB-approved Protocol Narrative
- Signed IRB-approved informed consent documents
- Subject enrollment records
- Subject case history
- Subject Medical Records
- Case Report Forms or electronic transfer of subject data, as applicable
- Sponsor correspondence [amendments, modifications], as applicable
- IRB correspondence [amendments, modifications, renewals]
- Adverse Events reported to the IRB and sponsor, as applicable
- Subject encounters with dates of service
- Agreement between UCI and sponsor approved by Sponsored Projects Administration, if applicable
- Investigational article (drug, device, radio-isotopes, etc.) records
- Investigational drug dispensing records, as applicable
- BioSci 199 student files, as applicable
- At the time of the audit, subject files from each protocol will be randomly selected from the protocol enrollment logs.

# Protocol Audit Tool

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## RESEARCH PROTOCOL AUDIT TOOL

### TABLE OF CONTENTS

I.	<b>General Investigator / Protocol Information</b>	01
II.	<b>Sponsor Regulatory File</b>	02
	General Observations	02
	Communications with Sponsor	03
	IRB Approvals	05
	Clinical Laboratory Testing	06
III.	<b>Administrative Approvals</b>	07
	Institutional Signature and Approval Documentation	07
	Sponsored Project Approval	07
	Case Report Forms	08
IV.	<b>Research Records</b>	09
V.	<b>Informed Consent and HIPAA Authorization</b>	11
VI.	<b>Record Documentation and Retention</b>	12
VII.	<b>Electronic Records &amp; E-signatures</b>	13
VIII.	<b>Computer Systems</b>	15
IX.	<b>Drug and Device Accountability</b>	23
X.	<b>Student Researchers</b>	25
XI.	<b>Tissue Repository</b>	28
XII.	<b>Reviewers Signatures</b>	30

***Audit tool is used for all audits. Tool can be modified to the type of research and protocol***

# Example of Audit Tool

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## INVESTIGATOR REGULATORY FILE

**Yes No N/A**

- Investigator's written protocol available
- Investigator's written protocol updates and/or revisions on file
- Instructions available for handling investigational product/s & trial-related materials [indicate if not included in protocol]
- Lead Researcher / co-Investigator curriculum vitae & other relevant documents on file
- New investigator curriculum vitae and updated FDA 1572 on file
- Protocol investigator and research staff signature sheet on file
- Notification by Investigator to IRB of Serious Adverse Events & related reports on file
- As appropriate, written IRB notification of any subject/s enrolled not meeting Inclusion or Exclusion criteria on file
- As appropriate, written notification (e.g., approved modification) from the IRB approving subject enrolled not meeting Inclusion/Exclusion criteria on file
- All concurrent illnesses and/or concomitant therapy documented on the study case report forms (CRF's)
- All screening failures, early terminations, dropouts; and, the reasons therefore, documented on the study enrollment log



# Completion of the Audit and Audit Report

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- *All protocol audits generate a compliance final report, report only findings supported by objective evidence*
- *Reports are detailed and list all applicable findings on audited protocols*
- *For routine audits, the entire protocol is audited against the sections applicable in the audit tool*
- *Prior to the completion of any final report, all research findings are discussed in detail with the PI and research staff*
- *Reports are sent to the PI, Chair, Dean of School of Medicine, IRB and others as applicable.*
- *If an audit has findings, a corrective action plan is always discussed and written as part of the report*

# Corrective Action Plans

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- *A corrective action plan is always included in the final report if audit findings require corrective action*
- *The correction action plan always references federal and state regulations, guidance documents, department policy, campus policy, sponsor agreements and protocol instructions*
- *A written response is required for an audit reported with findings and a corrective action plan*
- *Time limit to respond to audit report and implement corrective action plan*
- *IRB and other areas may include additional corrective action*
- *Follow up to see if corrective action plan was implemented and whether it was effective*

# Research Protocol Audit Program – Future Plans

- *Integrate clinical research billing audits with routine protocols audit*
- *Incorporate staff training including research coordinators as part of corrective action plan*
- *Implement metrics and best practices*
- *Revision of audit tool – add additional guidance*
- *Review 1<sup>st</sup> patient of all new protocols*
- *Compliance Office participation in protocol initiation meetings*

# Most Common Deficiencies Found

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- ***Failure to follow the investigational plan and/or regulations***
- ***Protocol deviations***
- ***Inadequate recordkeeping***
- ***Inadequate accountability for the investigational product***
- ***Inadequate communication with the IRB***
- ***Inadequate human subject protections – including informed consent issues***

*Taken from FDA Inspections Program Presentation, August 2012*

# *Thank You*

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