Beth Shields, MA, CIP, CCRA
Quality Assurance Coordinator
Human Research Protection Program (HRPP)
Quality Improvement Unit (QIU)
Beth.Shields@ucsf.edu
415-514-3823

UCSF
University of California
San Francisco
advancing health worldwide™

Human Research Protection Program

Quality Improvement Unit

Routine Site Visit Findings

August 7, 2012

UCSF
University of California
San Francisco

Agenda for Today

1. **Discuss the Routine Site Visit (RSV) purpose/goals, selection, and procedures**
2. **Review RSV Findings**
   - Discuss common examples of those findings
   - Provide suggestions for immediate action your team can take to ensure compliance
3. **Questions and Answers**

Human Research Protection Program

UCSF
University of California
San Francisco

Purpose of RSVs

- **To help *you*, our UCSF researchers, do your jobs even better!**
  - **Improve/ensure compliance**
    - Protocol and related procedures approved by CHR
    - Federal regulations, GCPs
    - State regulations
    - University guidelines
    - CHR policies and guidance
  - **Educate research staff**
    - Areas that research staff have questions about
    - Areas revealed during the RSV needing improvement
    - Resources available for education and training
    - Best practices (i.e., Good Clinical Practices)

Human Research Protection Program

UCSF
University of California
San Francisco

RSV Selection Process

- **Studies are identified for a RSV at the time of Continuing Review:**
  - Greater than minimal risk studies
  - Less than 5 years old
  - Participants are currently enrolled or being followed
  - Does not already have ongoing monitoring or auditing
- **Scheduled 1 - 6 months in advance**
- **A PI will be selected no more frequently than every 2 years**

Prior to the RSV…

The QIU Reviewer sends the PI and study contact(s) an e-mail with details about the visit, including a copy of the RSV review/report template.

Human Research Protection Program

UCSF
University of California
San Francisco

RSV Review Components – Part 1

Topics for Discussion with Research Team

- Staff roles
- Protocol implementation (including recruitment, consent, and protocol procedures)
- Data security
- Post-approval communication (CHR, Sponsor, FDA, etc.)

Human Research Protection Program

UCSF University of California San Francisco

RSV Review Components – Part 2

Review of Documents

- All or a subset of signed consent/assent documents
- Case report forms (also called “data collection forms”) and source documents for source document verification
- Regulatory binder, Sponsor correspondence, pre-iMedRIS CHR correspondence, etc.

Human Research Protection Program

UCSF University of California San Francisco

RSV Review Components – Part 3

Wrap-up

- Clarify questions from review of documents
- Provide overall assessment of study activities and protocol compliance
- Discuss specific findings, if any
- Discuss corrective actions that will be required/recommended based on findings
- Discuss ways to ensure compliance with regulatory requirements and GCPs for future studies
- Opportunity for questions and feedback on experience with CHR…

Human Research Protection Program

UCSF University of California San Francisco

After the Visit …

The QIU Reviewer writes a report which includes

- Evaluation of compliance with each area reviewed in the RSV (Yes, No, or N/A)
- Summary of discussion, focusing on significant areas of discussion
- Findings and Recommendations for improving compliance
- Summary Evaluation of Visit
  - Satisfactory, No QIU Recommendations
  - Satisfactory with QIU Recommendations
  - Significant Findings

The Research team reviews the report and responds to any QIU Recommendations that require follow-up

Human Research Protection Program

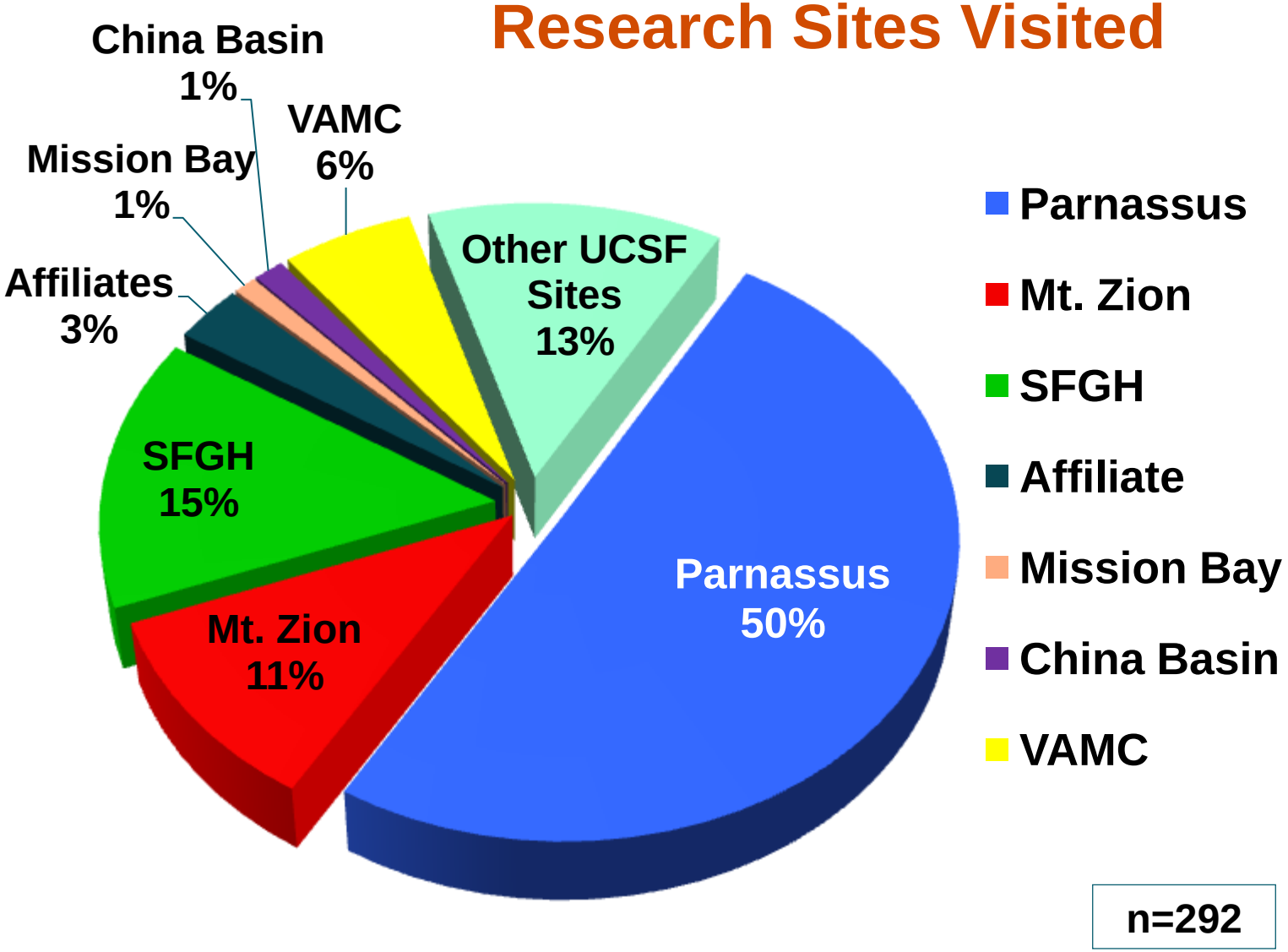
UCSF
University of California
San Francisco

RSV Findings
June 2008 – June 2012

Human
Research
Protection
Program

UCSF
University of California
San Francisco

Research Sites Visited

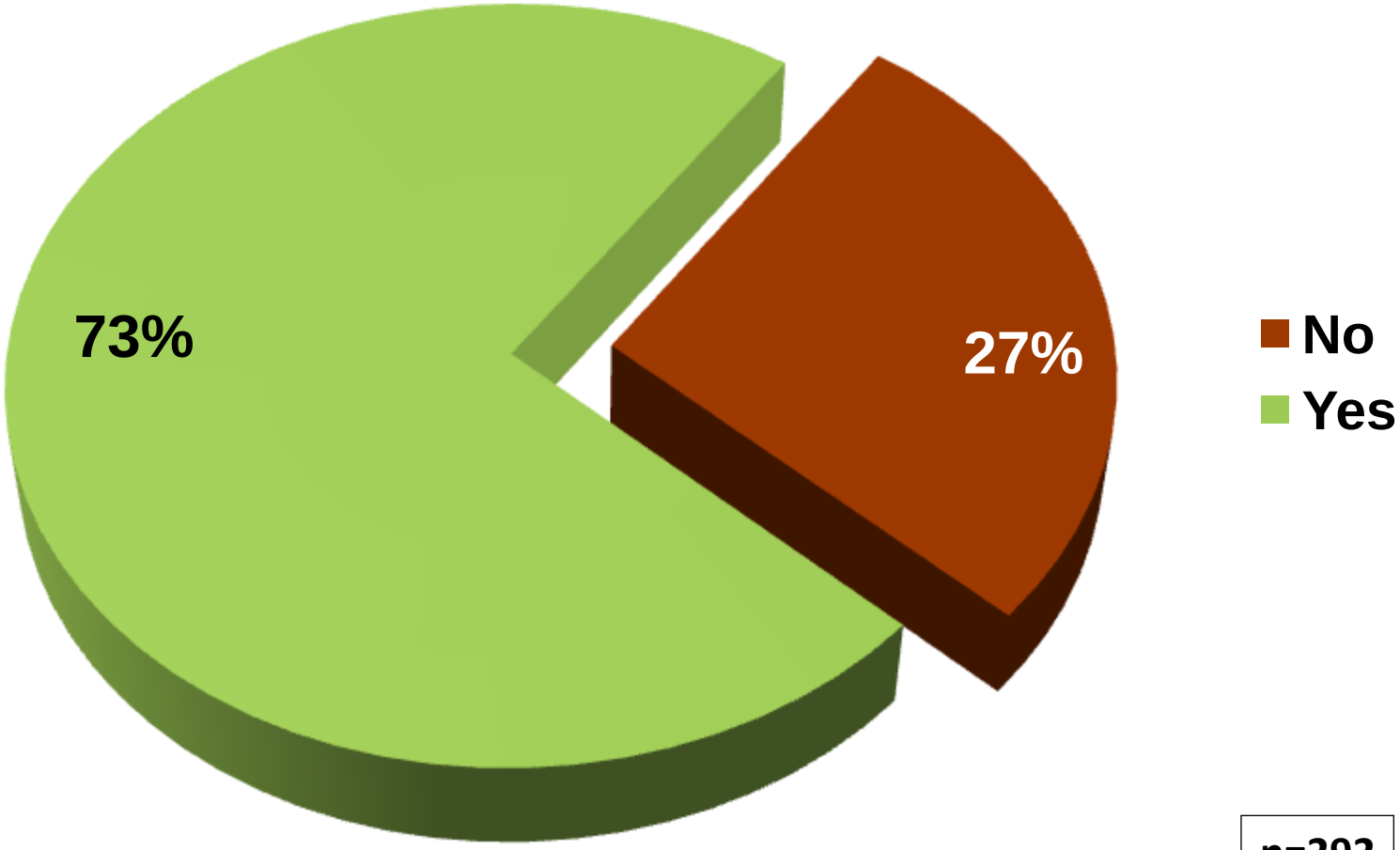


n=292

Human
Research
Protection
Program

UCSF
University of California
San Francisco

Have All Key Study Personnel (KSP) Completed/Updated CITI Training?



Human Research Protection Program

UCSF
University of California
San Francisco

Who are "Key Study Personnel"?

UCSF HRPP definition of KSP:

> Individuals who contribute in a substantive way to the execution and monitoring of the study at or on behalf of UCSF or affiliated institutions….In particular, investigators and staff involved in obtaining informed consent are considered key personnel *(emphasis mine)*

- Note that this is *not* the same definition that Sponsors use for the FDA 1572 or that NIH uses for grant applications.
- For the CHR application, KSP will often include people not on the grant application or FDA 1572 (e.g., research coordinators, research nurses) and will exclude people who are on those documents (e.g., MDs who assisted in the preparation of the manuscript but are not actively involved in carrying out the study).

Human Research Protection Program

UCSF
University of California
San Francisco

KSP Missing CITI Training

All KSP must complete the CITI online Human Subjects Protection Training course prior to working with research participants

- Some of the KSP have not taken or not completed the CITI course
- KSP took the course at another institution but have not transferred their affiliation to UCSF and have not taken UCSF modules

CITI course must be updated every 3 years

- Most common finding this year with regard to KSP is that they have not updated their training when it expired

Human Research Protection Program

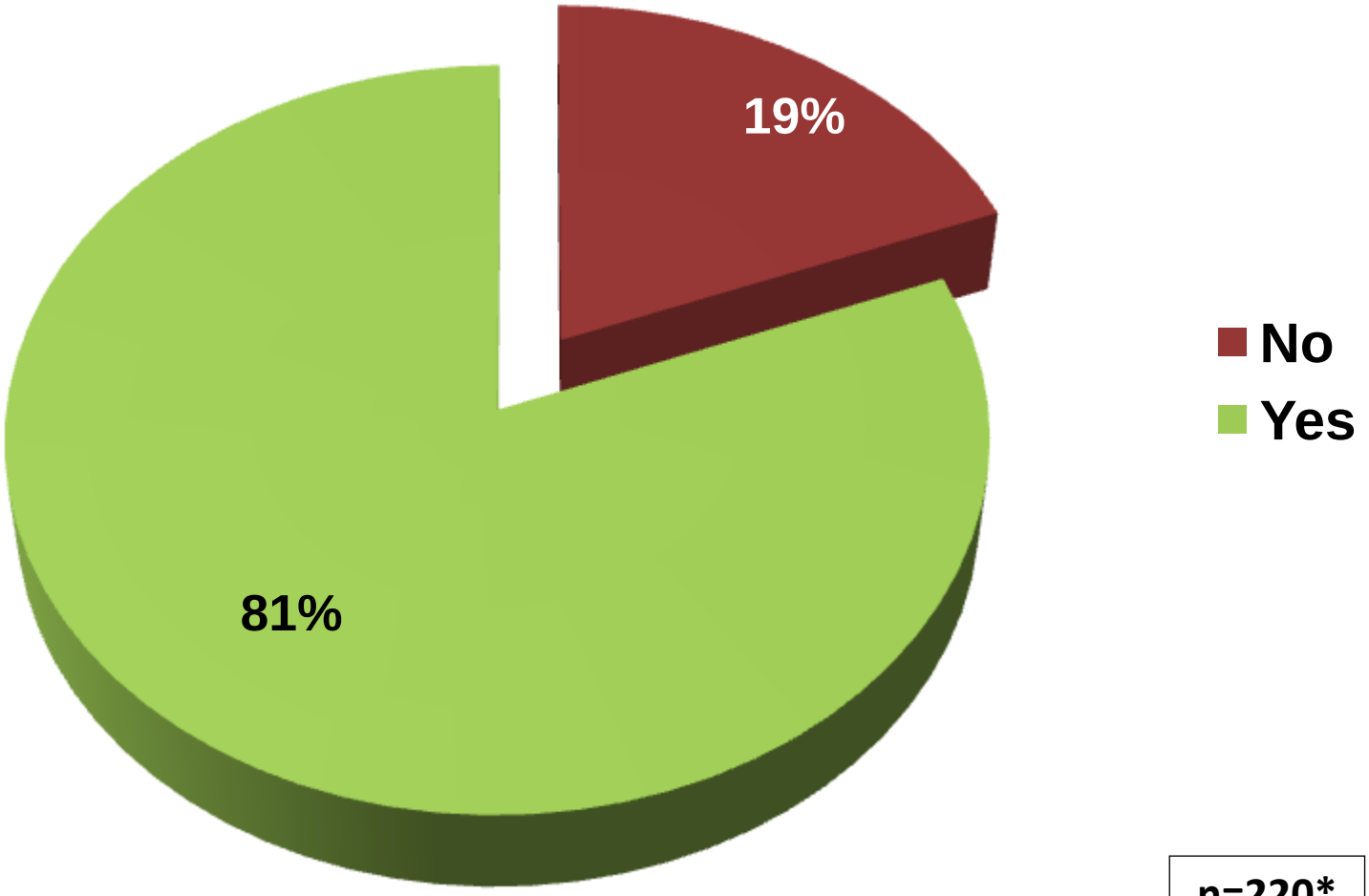
UCSF
University of California
San Francisco

How to Ensure that all KSP have Completed CITI Training

- Check the CITI Completion Page on the HRPP's website at: http://research.ucsf.edu/chr/Train/CITI_Training_Completed.pdf to keep track of CITI training completion and expiration dates.
- Consider assigning a team member to keep track of all KSP's CITI training expiration dates
- Hold all KSP responsible for keeping track of their CITI training expiration dates.

Human Research Protection Program

Are Study Procedures Conducted per Protocol?



n=220*

*This question was added to the QIU RSV form in March 2009

Human Research Protection Program

UCSF
University of California
San Francisco

Examples of Study Procedures not Conducted per Protocol

- Protocol states that all women of childbearing potential will have a urine pregnancy test performed at Week 1. The pregnancy test was not performed.
- Protocol states subjects will be randomized (by computer) into Group A or Group B. The procedure that was used was to enroll the first 15 subjects into Group A and the next 15 subjects into Group B.
- Protocol states that a MRI will be obtained a the Week 6 study visit. The investigator decided that the MRI was not necessary and therefore subjects were not having the MRI at Week 6.

Human Research Protection Program

UCSF University of California San Francisco

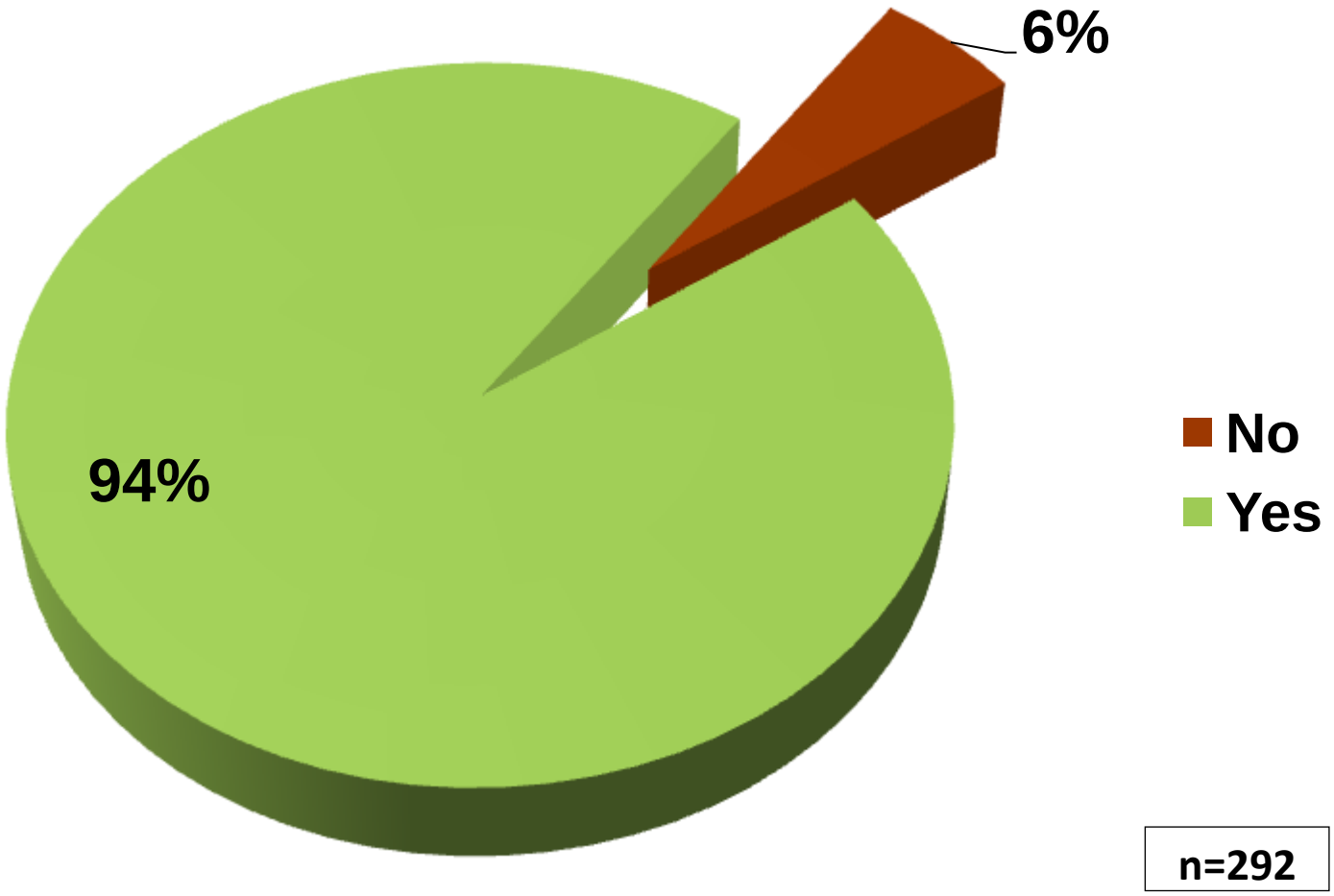
How to Ensure that you are Conducting Study Procedures per Protocol

- **Develop Standard Operating Procedures for all study procedures.**
  - If time doesn't permit, then develop SOPs for study procedures that are new/novel to this protocol and/or that have lots of room for error, e.g.:
    - Lots of steps
    - Lots of players
    - Lots of communication required
    - Complicated procedure
    - Procedures done with non-UCSF staff
- **Develop other tools that will help the team be successful, e.g.:**
  - study calendars,
  - pocket guides (e.g., inclusion/exclusion criteria, study contacts,)
  - standard MD orders, etc.

Human Research Protection Program

UCSF
University of California
San Francisco

Are Recruitment Activities per Protocol?



Human Research Protection Program

UCSF
University of California
San Francisco

Examples of Recruitment Procedures not Conducted per Protocol

- Protocol states that recruitment will be done by physicians during the clinic visit. Subjects were being recruited by research assistants in the clinic waiting room.
- Protocol states that potential subjects will be identified by chart review and sent a letter to notify them of the study. The research team was contacting potential subjects directly by phone.
- Recruitment materials (e.g., letters, flyers) had not been submitted to the CHR for approval.

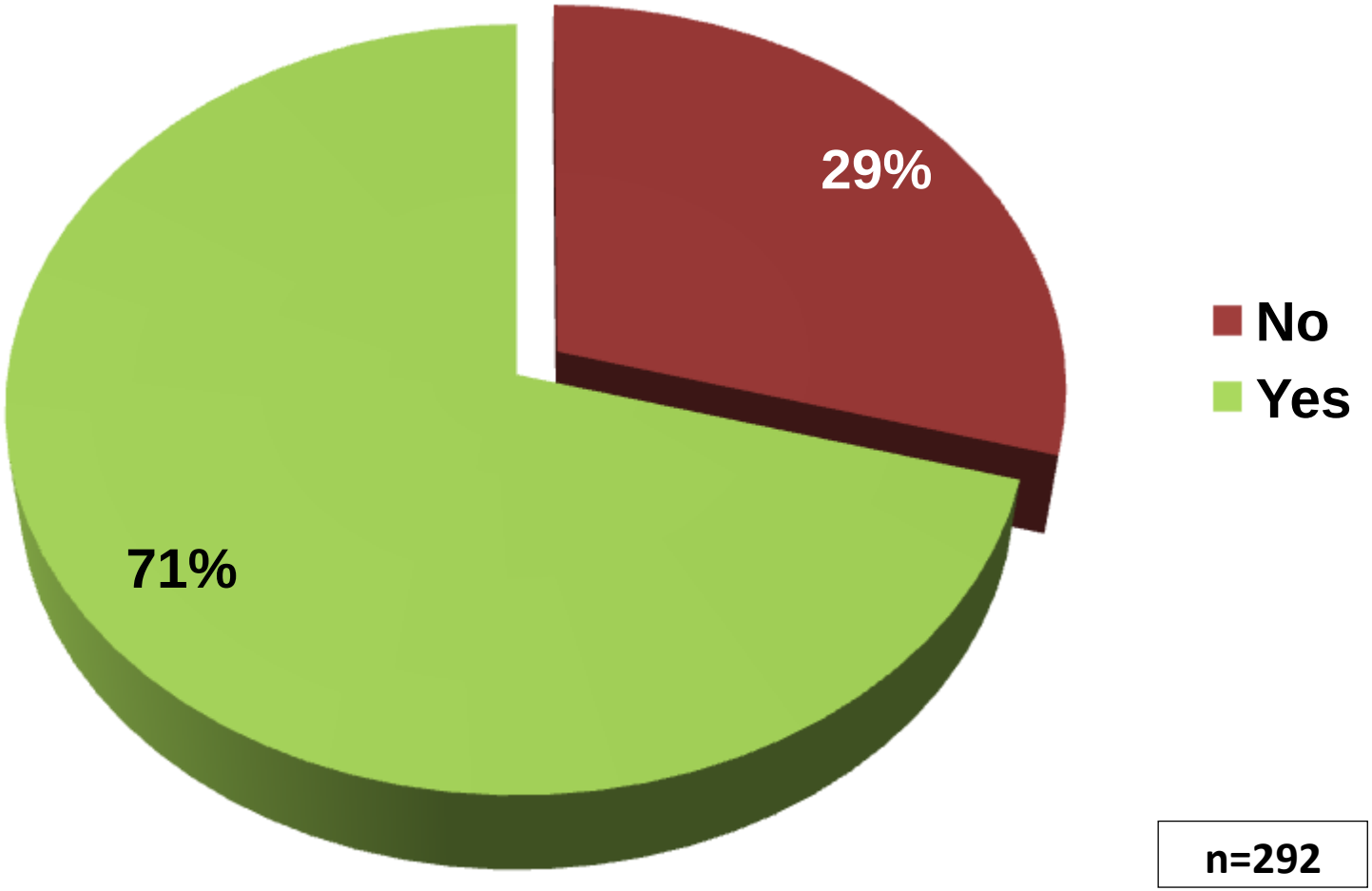
Human Research Protection Program

UCSF University of California San Francisco

How to Ensure that Recruitment Activities are per Protocol

- Make sure that all staff who are involved with recruitment know the approved procedures for recruiting subjects
  - Who may be recruited (adults, minors, non-English-speaking, etc.)
  - Where they may be recruited (clinic, support group, etc.)
  - By whom they may be recruited
  - How they may be recruited (in person, letter, phone call, etc.)
- Make sure that recruitment materials are approved by CHR
  - Review iMedRIS “Other Documents” for approvals
- If doing chart review or recruiting practitioners own subjects, be sure that you have a Waiver of Consent/Authorization for Recruitment from CHR.

Is the Correct Version of Consent Form Used?



n=292

Human Research Protection Program

UCSF
University of California
San Francisco

Examples of Use of Incorrect Version of Consent Form

- Subjects were enrolled with a version of the consent form that was not the most current version at the time they were consented.
- Subjects were enrolled with a version of the consent form that had not been submitted to but not yet approved by the CHR.
- Subjects were enrolled using a consent form that was for a different but similar study. The person obtaining consent had not looked at the title at the top of the consent form and had not reviewed the document carefully with the subject at the time he obtained consent.

Human Research Protection Program

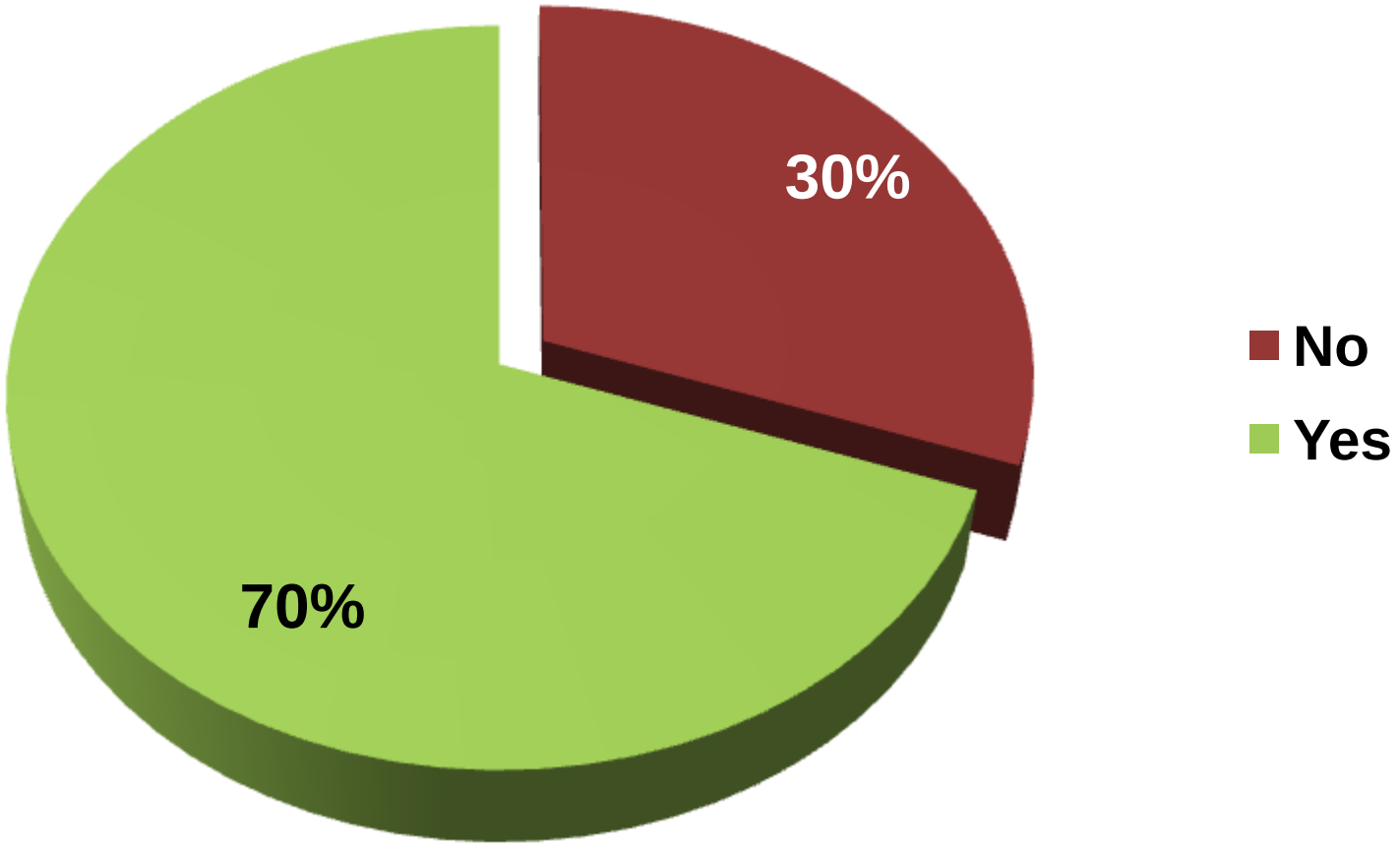
UCSF University of California San Francisco

How to Ensure that you use the Correct Version of the Consent Form

- Print the Consent form from iMedRIS when enrolling a subject.
  - All outdated versions of the Consent form in iMedRIS have “Void” stamped across the page
- Designate one person to ensure that the Consent form is distributed
  - Send a specially agreed upon e-mail to all staff with the new Consent form attached
  - Go to enrollment sites to replace old versions of consent with new version
- Look at the header on Consent to ensure that the version you are using is not expired
- Read the Consent form to make sure it accurately describes the procedures, risks, etc.
  - If not, you are most likely using an outdated Consent form.

Human Research Protection Program

Is the Consent Process Adequately Documented?



n=292

Human Research Protection Program

UCSF
University of California
San Francisco

Examples of the Consent Process not Adequately Documented

- The person obtaining consent did not sign the consent form.
- The person obtaining consent signed the consent form on a different date than the subject and there was no explanation why the dates were different.
- The person obtaining consent crossed out the CT scan listed in the “Procedures” section of the consent form.
- On a consent form that had a section for “Optional Procedures,” the subject did not indicate his/her preference regarding participating in the optional procedures.

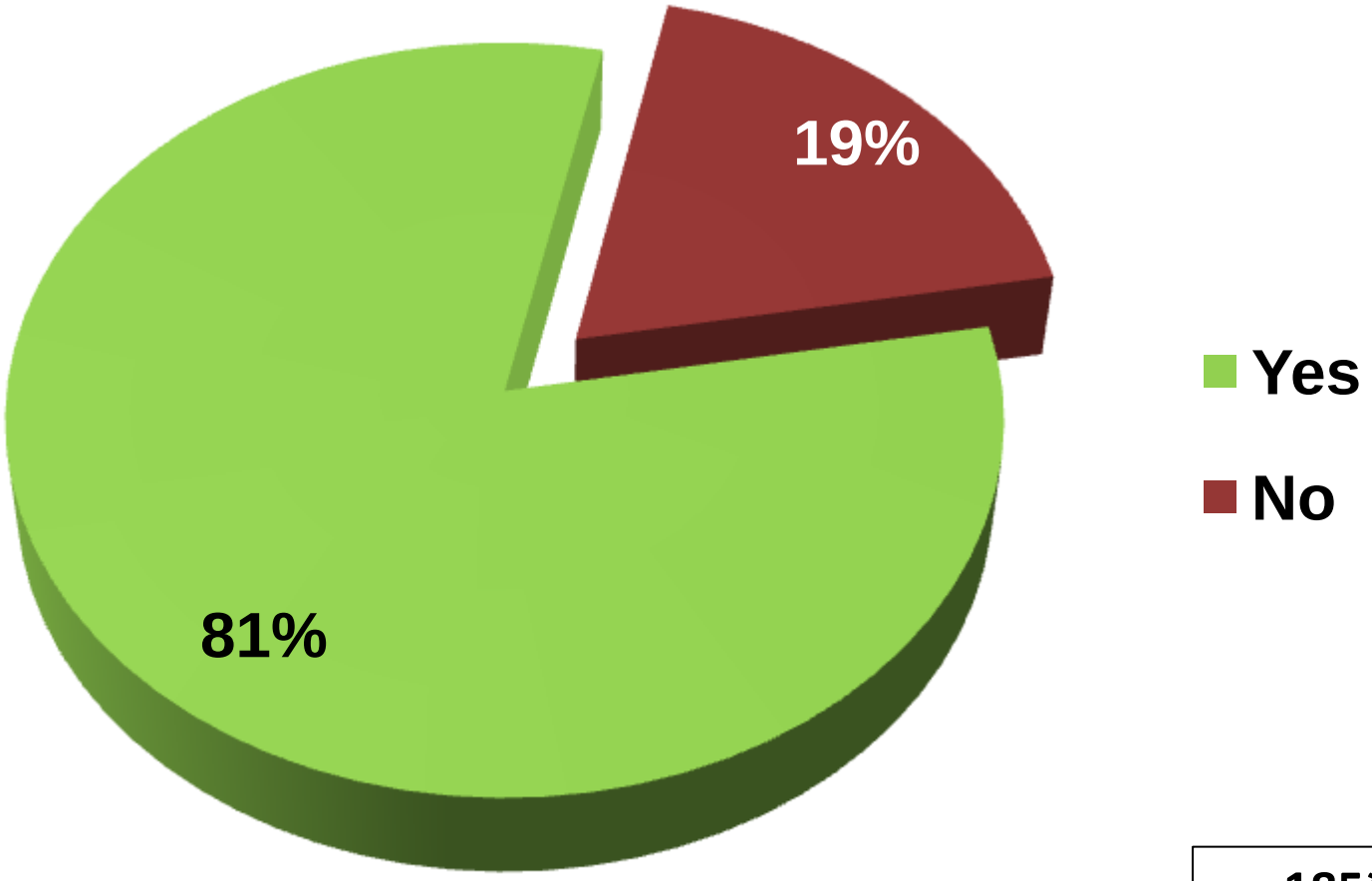
Human Research Protection Program

UCSF
University of California
San Francisco

How to Ensure that you Document the Consent Process Correctly

- Prior to copying the documents for the subject, make sure that all of the lines in the Consent block have been filled in correctly and completely
- If the dates of the signatures are discrepant, make a “Note to File” describing why
- Never cross out any sections of the Consent form, even if a subject will not be participating in that portion of the study.
  - If you find that you need to cross out sections of the Consent form, you may need to modify your protocol and Consent form.
- Prior to signing the Consent form, review it to make sure that all “Optional Procedures” boxes have been initialed/checked

Does the Consent Form Accurately Represent the Study Protocol?



n = 185*

* This number reflects a selected group of Consent Forms reviewed as part of the QIU RSV process

Human Research Protection Program

UCSF
University of California
San Francisco

Examples of the Consent Form not Matching the Protocol

- The protocol was modified to remove a study procedure. The procedure is still listed in the Study Visit table at the end of the consent form.
- The protocol was modified to increase the number of subjects in the study. The number of subjects participating in the study was not changed on the consent form.
- An additional funding source was obtained but was added to the Consent form in the Funding section but not to the Confidentiality section.

Human Research Protection Program

UCSF
University of California
San Francisco

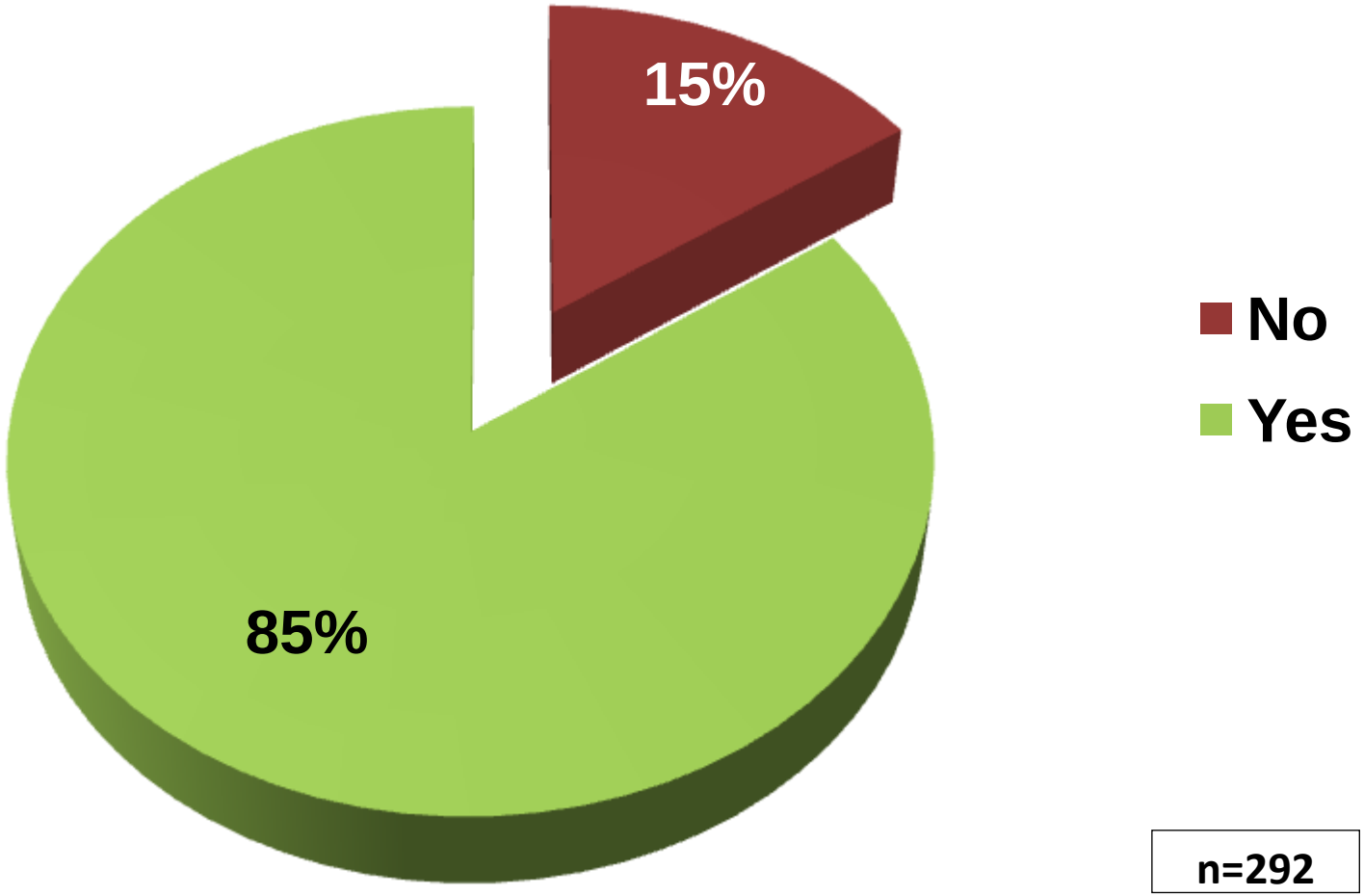
How to Ensure that your Consent Form always Matches your Protocol

- **Anytime that you modify your protocol, consider whether or not the modification affects the Consent/Assent form.**
  - If you have multiple Consent forms, make the change(s) in all of them.
  - Consider that the modification may require changes to multiple sections in the Consent form (e.g., Procedures and Risks).
  - If you have foreign language Consent forms, these will also need to be revised and resubmitted.

Human Research Protection Program

UCSF
University of California
San Francisco

Were Modifications Approved prior to Implementation?



n=292

Human Research Protection Program

UCSF University of California San Francisco

Examples of Modifications Implemented prior to CHR Approval

- The PI decides not to do a blood draw that is listed in the protocol and Consent form because it is not necessary for the study.
  - Removing procedures (as well as adding them) is a modification to the protocol
- A funding source is deleted from the Consent form
  - This is a modification to the protocol and needs to be submitted to the CHR before changing the Consent form
  - Some changes, e.g., updating a phone number, are permissible.
- The study team decides to provide subjects with an additional $10 to cover transportation costs. They submit a Modification to the CHR and immediately begin providing the additional compensation.

UCSF University of California San Francisco

How to Ensure that you don't Implement Modifications Prior to CHR Approval

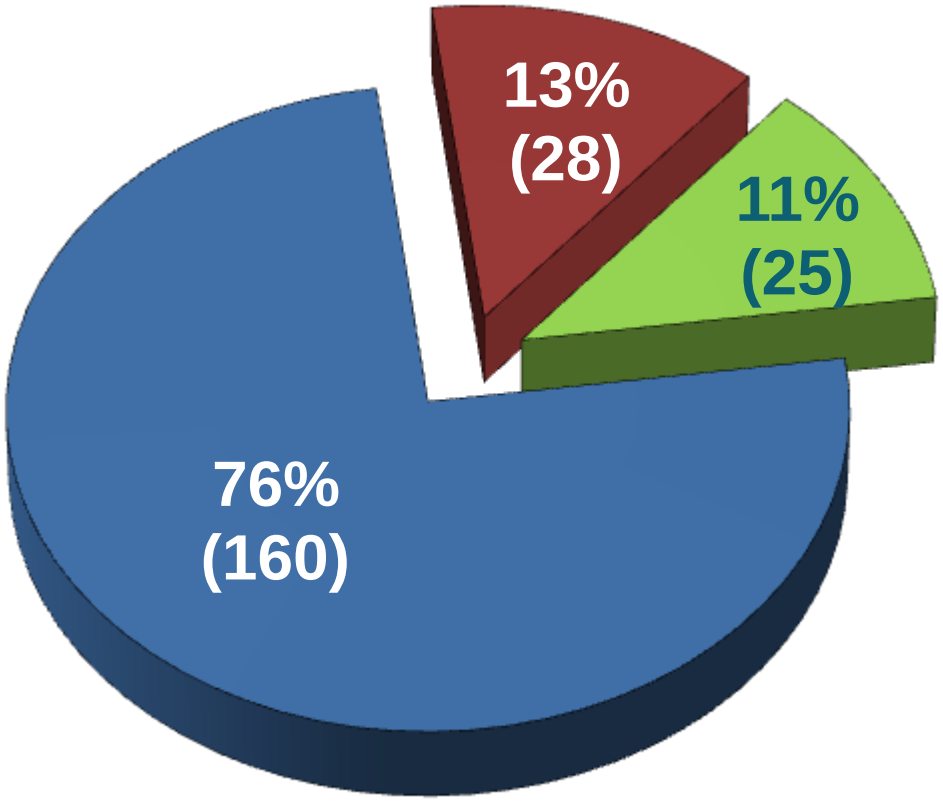
Changes to the protocol must be reviewed and approved by the CHR prior to implementation.

- Have frequent team meetings to discuss the study progress and procedures. Determine if modifications are needed.
- Do not implement modifications to the protocol until you have received notice of CHR approval.
- Appoint a team member (or the PI) to be in charge of letting the rest of the team know when the modification has been approved and it can be implemented.

Human Research Protection Program

UCSF
University of California
San Francisco

Overall RSV Summary Evaluation



n=292

Human Research Protection Program

UCSF
University of California
San Francisco

RSV: Satisfactory with Recommendations

- **Suggestions to improve study documentation or implementation**
- **Minor incidents and deviations from the CHR-approved protocol**
- **Examples:**
  - Key Study Personnel needed to complete or update their required CITI training.
  - Subjects had signed the incorrect version of the consent and changes were minor.
  - Follow-up to Conditions or Comments on CHR approval letters not addressed.
  - A procedure was no longer being done but had not been removed from the protocol or Consent form.

Human Research Protection Program

UCSF University of California San Francisco

RSV: Significant Findings

- **Major violations with the conduct of the study based on the CHR approved protocol**
- **Risks to subjects increased because of study conduct**
- **Examples:**
  - HIPAA Violation: accessing medical records without obtaining signed HIPAA Authorization and without an approved Waiver of Authorization from the CHR
    - Your approval letter will let you know if you need to obtain HIPAA Authorization from subjects who participate in the study.
    - If you are obtaining information from or putting information into the subject's medical record, you need to obtain Authorization.
  - CHR Application and consent form did not describe a major study procedure
  - Non-English speakers, minors, prisoners, or cognitively impaired subjects were enrolled without CHR approval
  - Subjects had signed the incorrect (older) version of the consent form, which included major changes in the study procedures

UCSF
University of California
San Francisco

Quality Improvement Unit

- **Lisa Denney, MPH, CIP, CCRP**
  Assistant Director
  Quality Improvement Unit (QIU)
  Lisa.Denney@ucsf.edu (415) 514-2152
- **Laurie Herraiz, RD, CCRP**
  Quality Assurance Coordinator
  Laurie.Herriaz@ucsf.edu (415) 514-9246
- **Melanie Mace, MA, CIP, CCRA**
  Education and Training Coordinator
  Melanie.Mace@ucsf.edu (415) 476-9839
- **Beth Shields, MA, CIP, CCRA**
  Quality Assurance Coordinator
  Beth.Shields@ucsf.edu (415) 514-3823

Human Research Protection Program

UCSF
University of California
San Francisco

Resources

- **HRPP Website:** http://research.ucsf.edu/chr/
  - QIU Section of HRPP Website:
    - http://research.ucsf.edu/chr/Qip/hsppQip.asp
  - Education Section of HRPP Website:
    - http://research.ucsf.edu/chr/Train/chrTrain.asp
- **UCSF HUB Website**
  - http://hub.ucsf.edu/
- **Clinical Research Coordinators Website**
  - http://research.ucsf.edu/chr/Train/CRC_Group.asp
- **ICH E6 Good Clinical Practices**
  - http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf
- **FDA Warning Letters**
  - http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm

UCSF
University of California
San Francisco

Acknowledgements

Lisa Denney, MPH, CIP, CCRP

Laurie Herraiz, RD, CCRP

Human
Research
Protection
Program

UCSF
University of California
San Francisco

Upcoming CHR Classes

CHR Intro Training: Protecting Human Subjects

Thursday, September 18, **10:00 am – 12:00 pm**

iMedRIS Classes

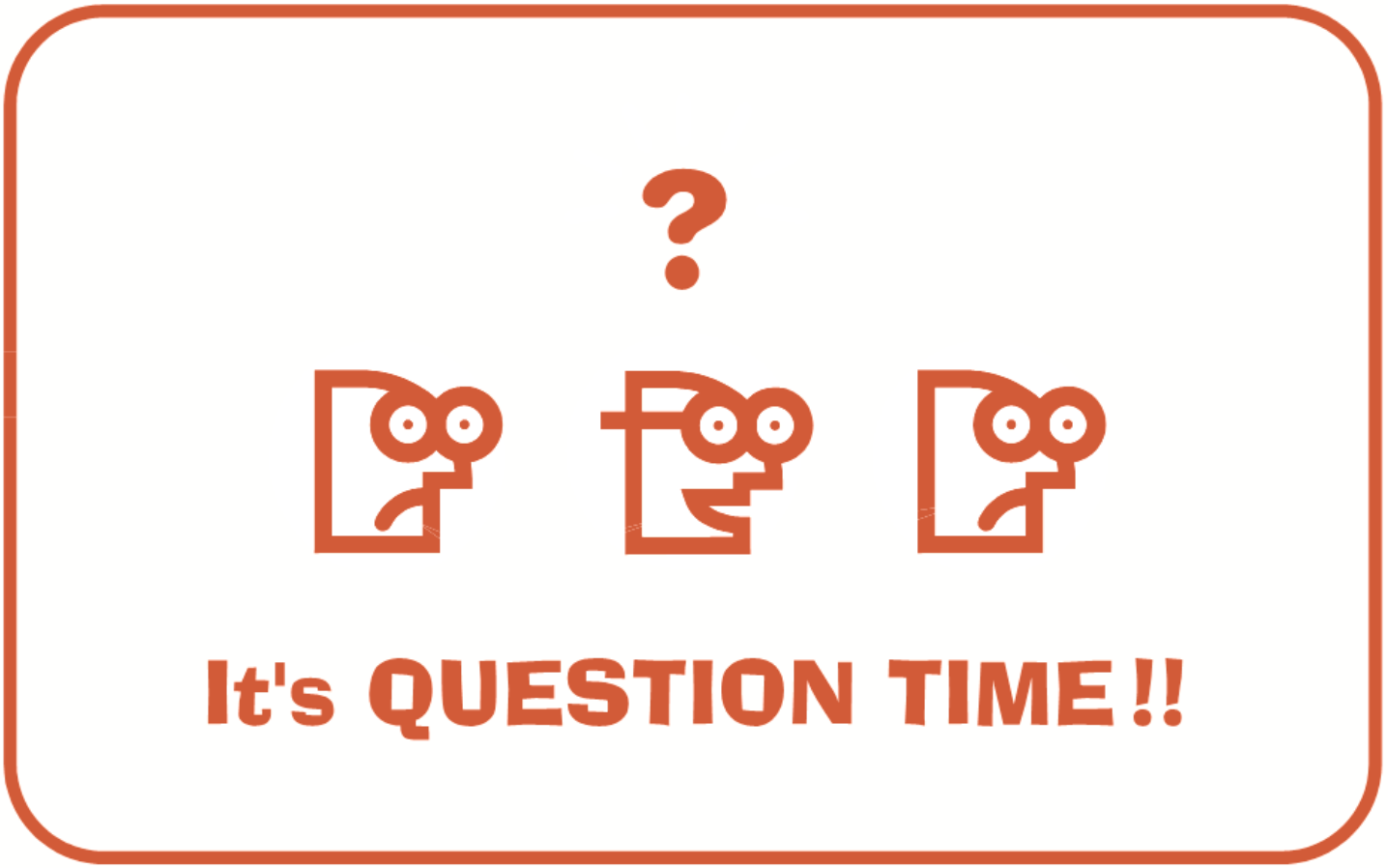
- **Managing Approved Studies in iMedRIS**
  - Thursday, September 13, **10:00 – 11:30 am**
- **Introduction to iMedRIS**
  - Tuesday, August 21, **9:00 – 10:30 am**

See HRPP Website to register for these classes and to find more education opportunities:

http://research.ucsf.edu/chr/

Human Research Protection Program

UCSF
University of California
San Francisco



Human
Research
Protection
Program