The ORARC Quality Improvement Program (QIP) Can Help!

- **QIP Services**
  - QIP Consultation
  - IRB/ESTR Submission Assistance
  - Study Management Tools (e.g., logs and Regulatory Binder)
  - Investigator/Study Staff Training
  - QIP Monthly Education Series (see website for details)

- **QIP Service Request Form**

- **QIP Education Sessions**
  - Don’t Let Research Misconduct Ruin Your Career: What is research misconduct and how to avoid it

*Contact QIP with any little (or big) question at all!*
Auditing & Reporting Slip-ups When Conducting Human Research

Reporting Requirements, Submitting RNIs, and Common Audit Findings

Julie Chamberlin, MPH, CCRP, CIP
IRB Reliance & QA/QI Specialist
&
Alyssa Speier, MS, CIP
QIP Director
Why report? Regulations!*

- DHHS & FDA regulations [*45 CFR 46.108(4)(i) & 21 CFR 56.108(b)(1)] require that IRBs have:
  - Written procedures for ensuring prompt reporting of
    - a) any unanticipated problems,
    - b) serious continuing noncompliance, or
    - c) a suspension/termination of the study

- DHHS & FDA regulations [*45 CFR 46.108(3)(iii) & 21 CFR 50.25(b)(5)] require that IRBs evaluate new information that becomes available during a study which may require the IRB/Investigator to reassess the risk/benefit to participant.
What should be reported?

- New or Increased Risk
- Adverse Events (Internal & External)
- Findings/Allegations of Regulatory Non-Compliance
- Audits/Inspections by Federal Agency
- Protocol Deviations/Violations
- Breach of Confidentiality
- Participant Complaints
- Protocol Suspension/Termination
When should I report?

- Within 5 business days from the time the study team became aware of the information
Where should I report?

- All reporting should be done in ESTR via a Reportable New Information (RNI) Submission.
ESTR RNI Submission – Key Elements

- Date PI became aware of the information
- Category of the new information
- Description of the occurrence/incident
- If (and why) the incident/new information in the PI’s opinion:
  - Poses a change to the study risk(s)
  - Requires a modification to the approved research
- Corrective Action Plan
  - PI is encouraged to propose a plan
  - IRB Review Specialist (and QIP, if engaged) will weigh in
  - Convened IRB, if engaged, will weigh in
Corrective Action Plans

- Should include corrective actions and preventative actions

- Corrective actions would include:
  - RNI
  - Disclosure
  - Study Audit

- Preventive actions would include:
  - Modifications to protocol
  - Modifications to consent
  - Re-consent of participants
  - Re-training of staff
Once submitted the RNI will first be reviewed by your IRB Review Specialist.

You may be asked for further clarification and details about the information you provided in ESTR.

The IRB Review Specialist will consider whether the incident is
- An unanticipated problem involving risk to subjects or others
- Serious noncompliance
- Continuing noncompliance

If the RNI involves any of the above 3 designations it will be reviewed at an IRB meeting by the full board.
Who should submit *report*?

- Any study team member listed in ESTR can submit an RNI for a study they are affiliated with.
  - If the RNI goes to a convened IRB meeting for review and/or results in an official IRB correspondence letter, this will be addressed to the PI of the study and cc’d to any relevant parties (e.g. Dept. Chair, SPA, Funding Sponsor, Federal Agency, etc).

- The IRB can submit an RNI as needed to report on a study
Case Study #1

- A research assistant is traveling for work with their personal laptop which they also use for their research. The RA uses this laptop to access REDCap and conducts their analysis of data on a dedicated HSPH department server specifically for this study. The RA needs to use their Harvard Key to get into the server and their laptop requires a login/password to access. The RA’s bag is stolen at the airport along with their laptop.
Case Study #2

• A participant is in a study that requires them to wear an activity monitor that will collect data on their physical activity, heartrate, and sleeping. The participant starts getting a rash where they are wearing the device and after 4 days wearing the device they decide to take it off and stop with the data collection portion of the study. The participant notifies the study about this at the next study visit which is 2 weeks after they stop wearing the device.
A research study collects data from participants via an online survey and no identifiable information is being collected. The online survey is made up of various questionnaires. During the course of the study the research team realizes that they need a new questionnaire to further collect information about participants social media consumption habits so they add in another questionnaire. They collect the new social media consumption habits data from 200 participants before the new questionnaire was approved via a Modification.
Areas of Common Audit Findings

• IRB approval
  - Ensure that ALL needed approvals are in place
  - Read approval letters
  - Expiration date?

• Protocol deviations
  - SOPs needed?
  - Know your protocol!
  - Submit modifications

• Informed consent

• Study Files
  - Regulatory documentation
  - Participant Files
Avoid Protocol Deviations: Questions to ask yourself/your staff regularly

- Have the risks or benefits changed since the last submission to the IRB?
  - Have there been any adverse or unanticipated events, or discoveries that could impact the risks/benefits ratio of the study

- Is recruitment progressing as expected?
  - If recruitment is overly effective, you may need to submit a modification to amend the approved number of participants
  - If recruitment is slower than anticipated, you may consider a modification to add additional recruitment methods or study locations
Questions to ask yourself/your staff regularly

continued

- Are participants expressing any misunderstanding or confusion during the consent process?
  - Does the consent form or consent process need to be revised to increase understanding?

- Are data storage and transfer methods still adequate?
  - Is there enough physical file cabinet or digital storage space?
  - Have there been any issues with lost or misdirected data?

- Are there any concerns with the conduct of the study?
  - What does the data look like – any consistently missing values?
# What is Regulatory Documentation?

## All Studies:
- Protocol
- Staff CVs
- Training
- Staff Licensures
- IRB Documents
- Logs
- Consent Forms
- Data Collection

## Study-Specific:
- Lab Documents
- FDA
- Investigational Brochure
- Drug/Device
- NIH
- Sponsor
- DSMB
- Local Review

**Harvard Longwood Campus Template Regulatory Binder:**
[https://www.hsph.harvard.edu/regulatory-affairs-and-research-compliance/regulatory-binder/](https://www.hsph.harvard.edu/regulatory-affairs-and-research-compliance/regulatory-binder/)
Participant File Tips

• Maintain participant files securely and separate from the Regulatory Binder according to protocol

• Original signed consent documents
  - Depending on confidentiality provisions outlined in the Research Protocol, signed consent forms may be kept separate from the participant’s research data

• File completed data collection forms and source data

• Communication with participants
  - As above, depending on confidentiality provisions outlined in the Research Protocol, communication that includes identifiers may be kept with signed consent documents and separate from research data
Informed Consent Documentation Reminders

According to the protocol:

- Ensure Signed and dated
  - By participant (thumb print, mark?)
  - By person conducting the consent process
- All fields completed (e.g., participant ID number filled in where indicated)
- All check boxes completed
- Witness signature requirements met
- Assent conducted when appropriate/according to protocol
- Documentation of parental/guardian permission
- Documentation that copy of the IC was given to the participant
- Etc.
Consent Sample

Participant ID: 42

Statement of Consent
I have read the information in this consent form including risks and possible benefits. All my questions about the research have been answered to my satisfaction. I understand that I am free to withdraw at any time without penalty or loss of benefits to which I am otherwise entitled.

I consent to participate in the study.

SIGNATURE

Your signature below indicates your permission to take part in this research and to the use and disclosure of your protected health information:

Ward Bayston
Name of participant

Elizabeth Pelaney
Signature of person obtaining consent

Date
8-16-14

Date
8-18-14

Printed name of person obtaining consent
Tips for Successful Record Keeping

- Avoid maintaining duplicate records, particularly IRB documents
  - e.g., in ESTR, electronically on a shared drive, and hard copy in a paper-based Regulatory Binder

- Review documentation routinely
  - QIP recommends using the Investigator Self-Assessment as a guide when reviewing regulatory documentation

- Address and resolve documentation issues immediately upon discovery

- Customize the Regulatory Binder to meet the specific criteria for your study

- Maintain documents in a secure location (e.g., locked file cabinet, password protected computer)
More Tips for Successful Record Keeping

- Document and update materials in the Regulatory Binder in real time

- Use Study Management logs as appropriate (e.g., Enrollment log, Study staff signature and delegation log, etc.)

- Maintain documentation for at least 7 years from study closure date (Harvard Policy) or longer if sponsor requires
  - The Regulatory Binder and study documents, including participant files, must be maintained securely and readily available to auditors
Study Preparation:
Prepare Binders, Tools and Checklists

- Helps you to get and stay organized
- Ensures consistency and compliance
- Allows others to follow history of study
- Create prior to enrolling subjects
- Modify as study is amended/needed
A Note-to-File can reconcile many issues

When in doubt, write a note!

- Use to explain apparent discrepancies
- Use to identify location of files that are maintained outside of the Regulatory Binder (e.g., in electronic format on a shared drive or in ESTR)
- Each note-to-file should include the study number, PI name, date, and the initials of the person writing the note-to-file
Questions?

Quality Improvement Program (QIP) Staff

- Alyssa Speier, QIP Director, aspeier@hsph.harvard.edu
- Lisa Gabel, Senior QA/QI Specialist, lgabel@hsph.harvard.edu
- Amy Harchelroad, QA/QI Specialist, aharchelroad@hsph.harvard.edu

Department Assigned Review Specialist:

https://www.hsph.harvard.edu/regulatory-affairs-and-research-compliance/department-assignments/

IRB Reliance Specialist

- Julie Chamberlin, jchamberlin@hsph.harvard.edu

Additional Resources & Links

- ORARC Website: https://www.hsph.harvard.edu/orarc
- ORARC QIP Page: https://www.hsph.harvard.edu/regulatory-affairs-and-research-compliance/hlc-qip/
- ESTR Support and Training: http://estrsupport.fss.harvard.edu/home