HCCA Research Compliance Conference

Indiana University ClinicalTrials.gov Compliance Program

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Indiana University Office of Research Compliance

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Dual Compliance Concern

Factors  
Institutional Structure  
Stakeholders  
Regulatory Changes  
Policy Changes  
Compliance Initiatives

Administrators  
Administer Accounts  
Make Compliance Determinations  
Monitor Audit  
Train  
Report on Progress  
Address Inquiries

Researchers  
Record Registration  
Record Maintenance  
Results Reporting  
Approve & Release Actions  
Conduct Trial  
Capture & Organize Data

ClinicalTrials.gov (CT.gov)
Agenda

• Current Events
• Compliance Environment
  – Food and Drug Administration Amendments Act (FDAAA)
• Compliance Program
  – Indiana University (IU)
• Registration Process
• Monitoring Process
• Other Processes
  – Principal Investigator (PI)/Responsible Party (RP) Departure

BREAK

• Governance
• Collaboration: Institutional Structure and Elements of an Effective Compliance Program
  – Communication
  – Training and Education
• Questions? Discussion?

Current Events
STAT Investigation

“But while the industry generally performed poorly, major medical schools, teaching hospitals, and nonprofit groups did worse overall—many of them far worse.”

“The federal government has the power to impose fines on institutions...or suspend their research funding.”
“But it has not levied a single fine”.

“Reporting lapses betray research volunteers who assume personal risks based on the promise that they are contributing to public health...”.


STAT Investigation: Response

“To date, I have had approximately 20 CT scans for the trial—not one of which was good for me physically or psychologically, but all of which help researchers ascertain how the drug I take works. Yet the knowledge they gain from this study remains barren, if it does not circulate among other researchers, cancer doctors, and patients. I benefit from the study drug, but no one else will be aided unless at its conclusion the results of the trial are promptly reported not just in a medical journal but on the site provided for the dissemination of information required by law.”

“Apparently the F.D.A. can levy fines up to $10,000 a day per trial for late reporting; however, it has never penalized any institution or company for failing to post on ClinicalTrials.gov. Why would such a revenue opportunity...be lost?”

“...I remain fervent in my support of clinical trials. I am not alone among such supporters in believing that research investigators need to improve their accountability and transparency.”

“Thousands of patients have kept our side of the covenant. The researchers and the institutions for which they work should keep theirs.”

BMJ Analysis Across AMCs

“Only 29% (1245/4347) of completed clinical trials conducted by the faculty at major academic institutions were published within two years of study completion and only 13% (547/4347) reported results on ClinicalTrials.gov.”

“...no academic center published more than 40% of completed clinical trials within two years of completion or reported results for more than 41% of its trials.”

“...noticeable variation and poor performance across leading academic medical centers in the dissemination of clinical trial results.”

“The lack of timely reporting and publication fundamentally impairs the research enterprise, violates the commitment made by investigators to patients and funders, squanders precious time and resources, and threatens to compromise evidence based clinical decision making.”


BMJ Analysis Across AMCs: Response

“Of 299 AMC studies we checked from the shared data, only 214 (72%) correctly listed AMCs or their faculty as RP!”

“...the application of a self-created 2-year standard for completion of results reporting or study publication, combined with an inflated denominator, results in an inaccurate picture of the results-sharing performance of AMCs.”

“Results reported in ClinicalTrials.gov should be viewed with considerable caution and, absent peer-reviewed publication, should not be used as a basis for clinical care decisions.”

“These unfunded requirements cost the nation millions of “unseen” dollars annually. While that may be a wise investment, more open discussion of the benefits and drawbacks of proposed research rules and regulations, and far more careful, nuanced analyses are needed to further our common goals of ethically, economically, and responsibly advancing clinical science and fulfilling our public mission.”

Compliance Environment

Requirement and Definition

<table>
<thead>
<tr>
<th>Regulation</th>
<th>Timeline for Registration</th>
<th>Results Reporting Required</th>
<th>Penalty for Not Complying</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDAAA</td>
<td>21 days post first subject enrollment</td>
<td>Yes</td>
<td>Initial $10,000 and up to $10,000/day, withholding of funds, sanctions</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Regulation</th>
<th>Clinical Trial Definition/Inclusion Criteria</th>
</tr>
</thead>
</table>
| FDAAA | Trials of drugs and biologics*: (1) controlled; (2) clinical investigation; (3) other than a Phase I clinical investigation; (4) Food and Drug Administration (FDA) regulated. 

Trials of devices*: (1) prospective clinical study of health outcomes; (2) compares an intervention with a device against a control in human subjects; (3) FDA regulated; and (4) other than a small clinical trial to determine the feasibility of a device, or a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes 

OR 

Pediatric postmarket surveillance of a device |


Results Reporting

- Results reporting required for Applicable Clinical Trials (ACTs) when:
  - FDA regulated drug, biologic or device is approved, licensed or cleared
  - Primary Completion Date was 12+ months ago
    - Last subject received an intervention or examination
  OR
  - 30 days after FDA regulated drug, biologic or device is approved, licensed or cleared
- Results reporting is separate from publication
  - Results reporting rarely considered pre-publication
  **consult with specific journal**


Responsible Party

- Individual/entity responsible for registering and maintaining the record
- Identified as the individual/entity sponsoring or receiving funds for the clinical trial
- Per FDAAA, identified RP can delegate to the PI when the following are true:
  - Responsible for conducting trial
  - Access to and control over data
  - Right to publish results
  - Ability to meet all other requirements
- IU, when the RP, delegates to the PI

General Process

1. Obtain a PRS Account
   - Request Account (PRS*)

2. Complete, Approve and Release a New Record Registration
   - Responsible Party (IU PI)
   - Data Entry (PRS)
   - Data Review (PRS)

3. Receive a NCT**
   - Public Access (CT.gov)

*Protocol Registration and Results System
**National Clinical Trial #

FDAAA Clinical Trial Definition Review: Example #1

Issue:
- Standard of care for cancer is treatment A which is effective but can be damaging to certain organ systems

Hypothesis:
- A combination of FDA approved drugs A & B is as effective as the current standard of care while not damaging to organ systems

Additional Facts:
- All subjects receive the same intervention
- Study is evaluating the effectiveness of the FDA approved drugs A & B compared to the standard of care and its ability to not harm organ systems

Is this an ACT? Why or why not?
FDAAA Clinical Trial Definition Review: Example #2

Issue:
• When patients arrive at the ER with head trauma, standard of care is either drug A or drug B and the physician providing care will determine the drug utilized

Hypothesis:
• Drug B is more effective than drug A in alleviating the symptoms associated with head trauma

Additional Fact:
• The study investigator will review medical records for head trauma related symptoms reported by the patient up to 12 months after treatment in the ER

Is this an ACT? Why or why not?

Responsible Party Review: Examples

• Institution’s investigator holds the Investigational New Drug (IND)/Investigational Device Exemption (IDE) and is internally funded?
• IND/IDE holder and commercial entity funds trial conducted at institution?
• Institution participates in a multi-site trial and is not the coordinating center or recipient of National Institutes of Health (NIH) funding?
• Institution, non-IND/IDE trial is NIH funded?

Who or what entity is the RP?
Compliance Program

Landscape

- ClinicalTrials.gov support included 1 staff member in Clinical Trials Office
  - Completed Approve and Release actions
    - All records assigned to IU with exception of some IU investigator held IND/IDE trials
    - Had research community send all inquiries to PRS Help
    - No monitoring or auditing completed
    - No policies or internal documentation developed
- Indiana Clinical and Translational Sciences Institute (CTSI) prompted development of compliance program through engagement with IU Office of Research Compliance (ORC)
  - IU ORC, Quality Improvement Office (QIO) identified as functional office
  - Indiana CTSI identified as primary resource for scientific assistance
  - Stakeholders met continuously through compliance program development to review
Elements of an Effective Compliance Program

- Internal monitoring, auditing and reporting
- Compliance and practice standards
- Designated contact
- Training and education
- Response to offenses and corrective action
- Communication
- Enforcement

Development and Implementation
Policy

Scope
This policy applies to all Indiana University investigators acting as a Principal Investigator on an Applicable Clinical Trial (ACT).

Policy Statement
1. Regulatory Requirements
   A. Per Food and Drug Administration (FDA), Food and Drug Administration Amendments Act of 2007 (FDAAA 801), an ACT is required to register in a public registry and include results at the conclusion of the study.1
   B. Indiana University will comply with FDAAA 801 and utilize ClinicalTrials.gov as the public registry.

2. Responsible Party Role
   A. Per FDAAA 801, the responsible party role can be delegated from the sponsor to a qualified Principal Investigator1.
   B. For ACTs with Indiana University as the sponsor, Indiana University has delegated the responsible party role to the qualified Principal Investigator.

Reason for Policy
To foster a compliant environment that adheres to applicable federal regulations related to the registration and maintenance of ACTs in a public registry.

Responsibilities

• IU Responsibilities
  – Host compliance program

• IU ORC Operational Responsibilities
  – Administer accounts
  – ACT determinations
  – Monitor
  – Audit
  – Report
  – Train
  – Handle inquiries/concerns

• Research Community Operational Responsibilities
  – Identify RP
  – Create and maintain records
  – Attend or utilize training
  – Notify IU ORC of receipt of any correspondence from an external agency
  – Notify IU ORC of PI/RP personnel change

• Indiana CTSI Responsibilities
  – Provide assistance with scientific prompts
Transition Workflow

First 12 months of IR, CT gov Compliance Program

1. Sponsor Approves Action
   - No Notifications Sent and No Shipment Entry Completed

2. Status: Monitoring – Pending QIO
   - Modifications to CT gov Fields Required
   - Contact Study Team
   - Contact may include up to 4 Emails

3. Issue/Action Resolved

4. Issue/Action Not Resolved

After 12 months of IR, CT gov Compliance Program

1. Sponsor Approves Action

2. Status: Monitoring – Pending QIO
   - Modifications to CT gov Fields Required
   - Contact Study Team
   - Contact may include up to 4 Emails

3. Issue/Action Resolved

4. Issue/Action Not Resolved

Status: Monitoring – Completed
Website

Quality Improvement Office - ClinicalTrials.gov
Researcher Responsibilities

ClinicalTrials.gov Account Administration

Account Requests
Prior to all actions in ClinicalTrials.gov, an account is required and the account needs to be accessible by the account holder. Requests for new accounts need to be sent to ctep@nih.gov and include the following in the email:

- Full Name
- Username
- Email
- Phone
- Official Title

Requests for accounts that are no longer accessible by the account holder or require modifications need to be sent to ctep@nih.gov and include the following:

- Full Name
- Modification/Issue Description

Record Owner Modification
A Record Owner on an existing ClinicalTrials.gov record may need to be modified due to personnel or responsibility changes. Requests for a Record Owner modification need to be sent to ctep@nih.gov and include the following in the email:

- National Clinical Trial Number
- Institutional Review Board (IRB) Protocol Number
- Full name of new Record Owner

Website

Quality Improvement Office - ClinicalTrials.gov
Compliance Program Documentation, Regulations, Policies & Guidance

The Indiana University, ClinicalTrials.gov Compliance Program documentation, policy and SOP provide the framework in which monitoring and auditing of registration and maintenance in ClinicalTrials.gov will occur. Regulatory and policy documentation informs the operations of the Indiana University, ClinicalTrials.gov Compliance Program.

- Indiana University, ClinicalTrials.gov Compliance Plan
- Indiana University, ClinicalTrials.gov Policy
- Indiana University, ClinicalTrials.gov SOP

Indiana University SOPs for Research Involving Human Subjects is available on the Human Subjects Policies & Guidance page.

ClinicalTrials.gov Resources

- ClinicalTrials.gov Train Site
- ClinicalTrials.gov FDS Log In Site
- ClinicalTrials.gov Researchers Help Site
- ClinicalTrials.gov Training Materials

Federal Regulations and Guidance

- FDA, FDAAA, Title VIII, Section 501
- NIH, “Elaboration of Definitions of Responsible Party and Applicable Clinical Trial”
- FDA, 21 CFR 812
- FDA, Informed Consent Guidance
- Identifying an ACT under FDAAA/NIH Flow Chart
Website

Overview
- Record Owner completes ClinicalTrials.gov record
- Responsible Party receives automatic notification
- Responsible Party completes Approve action
- Responsible Party completes Release action
- Principal Investigator needs account in Protocol Results System

registration Process
Questionnaire

- ClinicalTrials.gov questionnaire in Kuali Coeus (KC) Institutional Review Board (IRB)
  - Available to all Expedited and Full Board new studies and renewals
- Question types include the following:
  - For all, does the protocol meet the definition of a clinical trial per NIH, FDA, International Committee of Medical Journal Editors (ICMJE)
  - For NIH, FDA, ICMJE, is registration pending, completed or not completed
  - For Centers for Medicare and Medicaid Services (CMS), if billing, is registration pending, completed or not completed
- KC IRB Questionnaire is a smart form and not all questions may be present depending on responses

Next steps: revise questionnaire based on upcoming regulatory and policy changes
## Questionnaire

1. **Internal document assists with ACT determination and administrative checks**

2. **Sections include:**
   - FDA regulated
   - Drug
     - Controlled
     - Clinical investigation
     - Other than a Phase I investigation
   - Device
     - Prospective clinical study of health outcomes
     - Compares an intervention with a device against a control in human subjects
     - Other than feasibility or prototype investigation
     - Pediatric postmarket surveillance
   - ACT determination
   - Administrative
     - KC IRB, CT.gov questionnaire
     - Informed consent documentation
### Notification: Registration

**Role:** IRB Protocol 

**Principal Investigator Name:**

As a part of the Indiana University, ClinicalTrials.gov Compliance program, the Office of Research Compliance performs regular monitoring on requirements and records. More information: [http://researchcompliance.iu.edu/ctsi/ptgov.html](http://researchcompliance.iu.edu/ctsi/ptgov.html).

**Action Needed:** Complete new record registration in the PIS.

1. If you do not have an account in the PIS, please request one by sending the following to ptgov@iu.edu:
   a. Full name
   b. Username
   c. Email
   d. Phone
   e. Official title
2. Please correctly identify the Principal Investigator.
3. If the Responsible Party, please complete the new record registration in the PIS. Assistance:
4. Please resolve by [insert due date].

If you have any questions, please contact the Indiana University ClinicalTrials.gov Administrator at ptgov@iu.edu.

Thank you.

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### Notification Schedule

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<td><strong>Research Community</strong></td>
<td>1st Email</td>
<td>Study Team, CTSI RKS Program Manager*, Business Manager (Late Results), Department/Division Chair (Late Results)</td>
<td>At Action/Issue Identification</td>
<td>2 Weeks</td>
</tr>
<tr>
<td><strong>Research Community</strong></td>
<td>2nd Email</td>
<td>Study Team, CTSI RKS Program Manager*, Business Manager (Late Results), Department/Division Chair (Late Results), Clinical Affairs AVP (Late Results, No Progress)</td>
<td>1 Week Post 1st Email, 1.5 Months Post 1st Email (Late Results)</td>
<td>1 Week</td>
</tr>
<tr>
<td><strong>Research Community</strong></td>
<td>3rd Email</td>
<td>Study Team, QIO AD, CTSI RKS Program Manager*, Business Manager (Late Results), Department/Division Chair (Late Results), Clinical Affairs AVP (Late Results)</td>
<td>2 Weeks Post 1st Email, 3 Months Post 1st Email (Late Results)</td>
<td>Due</td>
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• ORC AVP  
• QIO AD  
• CTSI RKS Program Manager*  
• Business Manager (Late Results)  
• Department/Division Chair (Late Results)  
• Clinical Affairs AVP | 3 Weeks Post 1st Email  
3.5 Months Post 1st Email (Late Results) | Overdue |
| HSO                    | Email  | • Study Team  
• HSO Screener | At Action/Issue Identification | No Due Date Provided  
Informed Consent Documentation Modifications Highly Prioritized |
| QIO                    | Email  | • QIO Staff Involved  
• QIO AD | At Issue Identification | 1 Week |
|                        | Meeting Request  | • QIO Staff Involved  
• QIO AD | 1 Week Post Email or After Continuous Issues | Due or Needed Due to Continuous Issues |

*CTSI RKS – Clinical and Translational Sciences Institute Regulatory Knowledge and Support

Note: Frequency and duration between notifications may change depending on the progress of the item. Depending on the item, it may not be escalated based on this schedule.

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## Monitoring Process
Monitoring Workflow

START

Research Community Function Monitored

Status: Monitoring - Pending QIO

Action/Issue Requiring Attention Not Identified

Issue/Action Resolved

Issue/Action Not Resolved

Contact Study Team

Status: Monitoring - Pending Res. Comm.

Status: Monitoring - Pending Clinical Affairs

Issue/Action Resolved

Status: Monitoring - Completed

Contact may Include up to 4 Emails

Problems and Planning Report

ClinicalTrials.gov PRS
Protocol Registration and Results System

Quick Links

New Record
Admin Quick Reference
Problem Resolution Guide

Record List

All Records Problem Records Custom Filter

Showing 1 records per page

Download the record list in a comma-separated values (.csv) file? Only the displayed columns will be included.

Selection: Problem Records

Record count: 0

Download Cancel
Monitoring Schedule

- **Research community**
  - Existing and active clinical trial registered on CT.gov (NCT # provided)
  - New clinical trial registered on CT.gov
    - ACT determination
  - Record Verification modified (12 months)
  - Results posted
  - Approve/Release action taken
  - Faculty turnover record reassignment or transfer
- **IU Human Subjects Office (HSO)**
  - KC IRB, CT.gov questionnaire
  - Informed Consent documentation
- **IU QIO**
  - Sending notifications and response to inquiries

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Notification: Responsible Party

Re: NCT Record 

IRB Protocol 

Principal Investigator Name 

As a part of the Indiana University, ClinicalTrials.gov Compliance program, the Office of Research Compliance performs regular monitoring on requirements and records. More information: [http://research.compliance.iu.edu/shop_citgov](http://research.compliance.iu.edu/shop_citgov) 

**Action Needed: modify the Responsible Party in the PRS record** 

1. If you do not have an account in the PRS, please request one by sending the following to citgov@iu.edu: 
   a. Full name 
   b. Username 
   c. Email 
   d. Phone 
   e. Official title 

2. Please correctly identify the Responsible Party: 
   a. If Indiana University is the Responsible Party, that role is delegated to the qualified Principal Investigator. More information: [http://research.compliance.iu.edu/shop_citgov](http://research.compliance.iu.edu/shop_citgov) 
   b. In the PRS record, please modify the Responsible Party. Assistance: [http://research.compliance.iu.edu/shop_citgov](http://research.compliance.iu.edu/shop_citgov) 
   c. Approve and Release assistance: [http://research.compliance.iu.edu/shop_citgov](http://research.compliance.iu.edu/shop_citgov) 
   d. Please confirm that all PRS record content is up-to-date and error-free. If modifications are required, please correct the inaccuracies. 
   e. Assistance: [http://research.compliance.iu.edu/shop_citgov](http://research.compliance.iu.edu/shop_citgov) 

4. Please resolve by [insert due date]. 

If you have any questions, please contact the Indiana University, ClinicalTrials.gov Administrator at citgov@iu.edu. 

Thank you.
Notification: Record Verification

Re: NCT Record #:
IRB Protocol #:
Principal Investigator Name:

As a part of the Indiana University, Clinical Trials.gov Compliance program, the Office of Research Compliance performs regular monitoring on requirements and records. More information: http://researchcompliance.iu.edu/policies-rules/irb.html

Action Needed: modify the Record Verification Date in the IRB record.

1. In the IRB record, please confirm that the content is up-to-date and error-free. If modifications are required, please correct the inaccuracies.
   Assistance: http://researchcompliance.iu.edu/policies-rules/irb.html
2. In the IRB record, please modify the Record Verification Date. Assistance: http://researchcompliance.iu.edu/policies-rules/irb.html
   b. PRS: https://register.clinicaltrials.gov/
   c. Note — if modifications made, the Record Verification Date will be automatically updated when the modifications are Released.
3. Please resolve by [insert due date].

If you have any questions, please contact the Indiana University, Clinical Trials.gov Administrator at ctgov@iu.edu.

Thank you.

Notification: Approve and Release

Re: NCT Record #:
IRB Protocol #:
Principal Investigator Name:

As a part of the Indiana University, Clinical Trials.gov Compliance program, the Office of Research Compliance performs regular monitoring on requirements and records. More information: http://researchcompliance.iu.edu/policies-rules/irb.html

Action Needed: the Record Owner made modification(s) to your PRS record. Approve and release the modification(s) to your PRS record.

1. In the PRS record, please approve and release the modification(s). Assistance: http://researchcompliance.iu.edu/policies-rules/irb.html
   PRS: https://register.clinicaltrials.gov/
2. Please resolve by [insert due date].

If you have any questions, please contact the Indiana University, Clinical Trials.gov Administrator at ctgov@iu.edu.

Thank you.
### Notification: Results

**Action Needed:** complete results reporting in the PRS.

1. Please confirm that the clinical trial meets the Applicable Clinical Trial definition AND results reporting requirements below:

#### Applicable Clinical Trial Definition

**Device** (must have ALL 4 or pediatric postmarket surveillance of a device):

- Prospective clinical study of health outcomes
- Comparator intervenes with a device against a control in human subjects
- FDA regulated
- Other than a small clinical trial to determine the feasibility of a device, or a clinical trial to test prototype devices where the primary outcome measure relates to feasibility and not to health outcomes

**OR**

- Pediatric postmarket surveillance of a device

#### Results Reporting Requirements

- FDA regulated drug, biologic, or device is approved, licensed or cleared
- Primary Completion Date was 12+ months ago

2. If the clinical trial meets the Applicable Clinical Trial definition AND results reporting requirements, please complete results reporting in the PRS. Assistance: [http://researchcompliance.iu.edu/webinars/ipcr_responsibility.html](http://researchcompliance.iu.edu/webinars/ipcr_responsibility.html)

   a. **PRS 1-on-1 Results Reporting Assistance**

   A member of the ClinicalTrials.gov results team can be available to help prepare you for results submission, orient you to the PRS (Protocol Registration and Results System), and walk you through the data entry process. If you would like to take advantage of this assistance, please send a request to the Lead Results Analyst, Heather Dobbins, using the general ClinicalTrials.gov email address: [register@clinicaltrials.gov](mailto:register@clinicaltrials.gov)

   They request that you include some available dates/times (including time zone) for an introductory call and the best phone number to reach you. Please copy [ips@iupui.edu](mailto:ips@iupui.edu) on your email.

3. If the clinical trial does **NOT** meet the Applicable Clinical Trial definition AND/OR results reporting requirements, please inform the Indiana University, ClinicalTrials.gov Administrator of your findings.

4. Please resolve by [insert due date].

Next steps: revise notification based on upcoming regulatory and policy changes

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CTSI RKS Program Manager*  
Business Manager (Late Results)  
Department/Division Chair (Late Results) | At Action/Issue Identification | 2 Weeks  
3 Months (Late Results) |
| Research Community     | 2nd Email | *Study Team*  
CTSI RKS Program Manager*  
Business Manager (Late Results)  
Department/Division Chair (Late Results)  
Clinical Affairs AVP (Late Results, No Progress) | 1 Week Post 1st Email  
1.5 Months Post 1st Email (Late Results) | 1 Week  
1.5 Months (Late Results) |
| Research Community     | 3rd Email | *Study Team*  
QIO AD  
CTSI RKS Program Manager*  
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<td>3 Weeks Post 1st Email</td>
<td>Overdue</td>
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<td></td>
<td></td>
<td></td>
<td>3.5 Months Post 1st Email (Late Results)</td>
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<tr>
<td>HSO</td>
<td>Email</td>
<td>Study Team, HSO Screener</td>
<td>At Action/Issue Identification</td>
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<tr>
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<td>QIO Staff Involved, QIO AD</td>
<td>1 Week Post Email or After Continuous Issues</td>
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Note: Frequency and duration between notifications may change depending on the progress of the item. Depending on the item, it may not be escalated based on this schedule.

## Other Processes
PI/RP Departure Action

- **Active Trial**
  - Complete modification to PI/RP
    - Notify newly assigned PI/RP of responsibilities
    - Modify record to reflect current clinical trial information
    - Exception: candidate for record transfer
      - Work with IU ORC to assist with record transfer process
  - Notify newly assigned PI/RP of responsibilities
  - Modify record to reflect current clinical trial information
  - Mark the record as completed/terminated/withdrawn
- **Trial Not Continuing**
  - Modify record to reflect current clinical trial information
  - Mark the record as completed/terminated/withdrawn
  - Results required?
    - Steps for modification to PI/RP or record transfer still required
  - Complete modifications and/or work with IU ORC on record transfer within the 30 days prior/14 days following

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**Record Transfer Flow**

Next steps: include additional steps based on recommendations from taskforce subgroup focused on PI/RP departures and institutional collaboration.
Record Transfer Review: Example #1

- Study is concluded
- Record is completed
- Results reporting required and currently created
- IND/IDE held by investigator and being taken to new institution

**What are the existing institution’s obligations?**

**Can this record be transferred?**

---

Record Transfer Review: Example #2

- Study is concluded
- Record is completed
- Results reporting required and currently created
- Existing institution recipient of NIH funds

**What are the existing institution’s obligations?**

**Can this record be transferred?**
Record Transfer Review: Example #3

- Study is open
- Record is active and open to enrollment
- NIH funding being transferred to new institution

What are the existing institution’s obligations?
Can this record be transferred?

Let’s take a break!
Governance

Advisory Committee

- **Committee Objectives and Structure**
  - Review the regulatory environment
  - Identify needed operational modifications
  - Meet twice a year and are presented all relevant data and updates
  - Not a decision making body, but instead serves an advisory role

- **Committee Membership**
  The committee is comprised of members selected from the following internal and external stakeholders:
  - IU ORC Leadership
  - IU HSO Leadership
  - Clinical Trials Contracting (CTC) and/or Clinical Trials Office (CTO) Leadership
  - Indiana CTSI Regulatory and System Expertise
  - Research Community Representation
Institutional Oversight Committee

- **Committee Objective**
  - Reviews ACT determinations when there is discord between the PI and the IU ORC and/or Indiana CTSI
  - Meets when an ACT determination need arises and is presented all relevant trial documentation
  - Is an ACT determination and decision making body

- **Committee Membership**
The committee is comprised of members selected from the following internal and external stake holders:
  - IU ORC Leadership
  - IU HSO Leadership
  - Indiana CTSI Regulatory Expertise
  - Research Community Representation

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**Notification: Oversight Committee**

Re: NCT Record #:
IRB Protocol #:
Principal Investigator Name:

Dear [insert name]:
The Indiana University Clinical Trials.gov Compliance program previously contacted you regarding posting results to your ClinicalTrials.gov record. You determined that the ClinicalTrials.gov record did not require posting of results due to the trial not being an Applicable Clinical Trial.

On [insert date] the Institutional ClinicalTrials.gov Oversight Committee met to review your trial and determine if the Applicable Clinical Trial determination is accurate. The committee determined that your trial is an Applicable Clinical Trial and that posting of results to your ClinicalTrials.gov record is required.

The below assistance is available both within and external to Indiana University as you post results to your ClinicalTrials.gov record:

- **Office of Research Compliance**
  [insert contact information]
  ctpov@iu.edu

- **Clinical and Translational Sciences Institute**
  [insert contact information]

- **Department of Biostatistics**
  [insert contact information]

- **ClinicalTrials.gov 1-on-1 Results Assistance**
  Contact [insert contact information] to facilitate
  ctgov@iu.edu

Please have results posted publically on ClinicalTrials.gov by [insert due date 3 months out].
Collaboration: Institutional Structure and Elements of an Effective Compliance Program

Collaboration between IU ORC and Indiana CTSI

- Overview
  - IU ORC: administer compliance program (monitoring, auditing, and training)
  - Indiana CTSI: assist investigators in meeting compliance obligations
- Collaborate on training/education and communication
Mission of the Indiana CTSI

- To increase translational biomedical research and improve the health of people of Indiana and beyond.
  - Regulatory Knowledge and Support Program:
    - provides assistance to investigators who need information and advice about federal, state and local human subjects research regulations, as well as assistance streamlining the protocol submission and review processes.

Key groups involved in collaboration

*Simplified org chart
Institutional Structure Scenarios

- Compliance office + CTSI
- Compliance office only
  - With or without a medical school
- Compliance program housed within IRB support
- Compliance program housed within medical school
- Non-academic medical center

**How can you engage stakeholders and what are the potential gaps?**

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Elements of an Effective Compliance Program

- Collaboration centered around:
  - Communication
  - Training and education

- Assist investigators on key issues:
  - Outcome measures
  - Results reporting
Why is Collaboration Necessary?

- Problem: investigators need targeted assistance in meeting compliance obligations
  - Engagement with investigators
  - Understanding obligations
  - Having the resources (time, assistance, tools, and training) to achieve compliance

Why is Collaboration Necessary?

Compliance policies, procedures, and committees are necessary but not sufficient

- PRS is a new process/unfamiliar system
- Different from activity required to publish
  - No narrative conclusions permitted, different timelines, often delegated to research coordinators
Effective Communication

• Avenues of communication:
  – Between administrators and investigators
  – Among administrators
  – Between administrators and leadership

Communication Scenarios

– PI has received 4 email notifications with no action (no response, no changes to study record).
– PI posts results, receives PRS review comments, and makes no changes to study record for 3 weeks.
– Research coordinator contacts compliance program administrator for assistance with registration. He wants to understand definitions and the PRS review process, as well as help writing outcome measures.
– Research coordinator contacts administrator because he has been delegated task of posting results. Coordinator faces challenges, and PI has been unavailable.

What is the next step? Are the appropriate parties involved?
Effective Communication

- Communication between administrators and investigators
  1. Notifications as outlined above
  2. Personalized follow up communications from CTSI targeting studies that have received PRS review comments
  3. Connection to PRS reviewers’ one-on-one assistance via conference call

Effective Communication: Personalized and Targeted

- Opens dialogue and provides additional contact
  - Send PDF of review comments for easy identification
  - Personalized message offering one-on-one assistance
Communication Example

• Follow up to notifications when PRS reviewers request revisions:
  – Brief, targeted, and review comments easily accessible
  – “In response to your results submission in November, a PRS reviewer posted review comments on December 10. For your reference, I’ve created a PDF of the results and their review comments, with the comments highlighted. Please feel free to contact me if you would like to discuss the review comments or if you are interested in having a conference call with a PRS reviewer.”

Communication Example

• Outcome measure assistance:
  – General comments (spell out acronyms, provide full range and description of all scales, etc.)
  – Specific to study:
    • E.g., “There should be one time frame per outcome measure. Since you are measuring efficacy at four time points, you could have four outcome measures – one for each time point (6 weeks, 6 months, 12 months, 24 months).”
  – Include screenshots for reference to specific data fields
Effective Communication

• Communication among administrators
  – Formal
    • Quarterly meetings with key administrators to review studies with late results
      – IU ORC
      – Indiana CTSI leadership
      – Biostatistics
    • Institutional Oversight Committee
      – Adjudicates disputed ACT determinations
  – Informal

Effective Communication

• Frequent formal and informal communications among stakeholders provides:
  – Continuous assessment of program and investigator progress
  – Identification of emerging issues
  – Opportunity to discuss solutions
Effective Communication

• Lessons learned:
  – Identify appropriate, influential notification recipients
    • In a decentralized academic institution, identifying appropriate stakeholders may be difficult
    • For late results, department/division chairs and business managers also receive notifications
  – Engaging investigators is instrumental

Next steps:
  – For new IITs: targeted communications offering assistance writing outcome measures
  – For late results: revised escalation plan with relevant sanctions for investigators
Training and Education Scenarios

– The research community asks for training.
– Research coordinators struggle with the PRS system.
– Coordinators attend training and mention that they wish their PIs would attend.

**How do you evaluate training needs?**

**What style of training would work best for your audience?**

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Training and Education: Increasing Awareness

• Departmental trainings
• Research coordinator training
  – Monthly sessions
  – Intermediate Coordinator Education Program
    • annual program targeting coordinators with 3+ years of experience
  – Professional organizations (SOCRA chapter meeting)
Training and Education: Interactive Training

- Hands-on PRS training:
  - Registration: 1.5 hours
  - Maintenance: 1 hours
  - Results: 2 hours

Training and Education: Collaboration

- Joint effort
  - Dual presenters
- Developed based on feedback and requests from research community, providing both:
  - What we think they need to know; and
  - What they’ve requested.
- Adapted training based on requests from research community
Training and Education

• What does training look like?
  – Computer lab setting
  – Combination of lecture and hands-on data entry
  – Developed short mock protocol with study results
  – Utilizes the PRS Test system for data entry
    • Created test accounts in PRS Test with mock study assigned to each account
    • Completed some data fields prior to training
    • Trainees complete missing data fields to orient to system

Training and Education

• Included in each session:
  – Introduction:
    • Relevant regulatory overview
    • System and Record Structure
  – Definitions of data fields
  – Screen shots of PRS modules
  – Data entry into mock study in PRS Test
Registration Training

- Handouts:
  - Mock Protocol
  - Slides
- Agenda:
  - System & Record Structure
  - Registration Module Completion
  - Resources (Biostatistics, contact information, etc.)

Registration Training Example Slides

Study Status
- Record Verification Date
  - Date record content last verified
  -Note: automatically set to current month and year
  - Tip: recommended to update every 4 months while recruiting
- Overall Recruitment Status
  - Overall accrual activity for protocol
- Study Start Date
  - Date enrollment in protocol begins
- Primary Completion Date
  - Date final subject was examined or received intervention for purposes of final collection of data
  - Tip: set to anticipated during new record registration
  - Note: this date has impact on when results are published
- Study Completion Date
  - Final data entry collected
  - Tip: set to anticipated during new record registration

Trainees enter data from mock protocol into PRS Test

Overview of data fields
- Definitions
- Tips
Registration Training Mock Protocol

A Phase 2, Single-Center, Randomized, Controlled Trial of Teens
Adults with Type 2 Diabetes
Study of Teens & Adults with Type 2 Diabetes (TADA)
Protocol INECTION trial (NCT01077796)
DATE: December 01, 2015
NCT ID: NCT017778

Parallel Study Design

One outcome measure

Maintenance Training

- Handouts
  - Mock Protocol
  - Slides
- Agenda
  - System and Record Structure
  - Federal Regulation Required Updates
  - Institutional Policy Required Updates
  - Utilizing Record List and Problems Report
  - Updates Needed for Results Reporting
  - Resources (Biostatistics, contact information, etc.)
Maintenance Training Example Slides

**Responsible Party**

- **Purpose**: the sponsor of the clinical trial or the principal investigator if so designated by a sponsor. Individual is responsible for conducting the trial, has access to and control over the data, the right to publish the results and ability to meet other requirements
- **Principal Investigator**: individual designated by sponsor
- **Sponsor Investigator**: individual initiates and conducts study
- **When**: at time of initial record registration or after monitoring notification sent from the Indiana University ClinicalTrials.gov Administrator
- **What**: every record requiring current or future approve and release actions in ClinicalTrials.gov
- **Why**: identified as an institutional requirement in the Indiana University, ClinicalTrials.gov Compliance Plan
- **Tip**: if Indiana University is not the sponsor, the registration will link to University ClinicalTrials.gov site

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**Results Training**

- **Based on template developed through collaboration of several CTSA institutions and the National Library of Medicine**

- **Handouts:**
  - Mock study results
  - Results templates from PRS Help menu
  - Slides

- **Agenda:**
  - Introduction
  - Results Reporting Requirement
  - Results Reporting Current Events
  - Preparing for Results Reporting
  - The Four Results Modules
    - Participant Flow
    - Baseline Characteristics
    - Outcome Measures
    - Adverse Events
  - CT.gov Review Process
  - Additional Resources
Results Training Example Slides

User-Specified Baseline Characteristics

- Do include all meaningful elements that make your study understandable/useful to others, both demographic and clinical measures, such as baseline values of outcome measures or prior and concurrent treatment characteristics.

- Make sure units and scales are labeled, and understandable – (e.g. what the range of a scale is and what it means. If it’s a well-known scale, within the discipline, refer to it by name and give a citation, if necessary.)

- Use Table 1, if there is a published article

- If there is no article from which to work

Enter Baseline Characteristics

Guidance and tips on results modules

Screenshots to orient trainees to modules

Enter Baseline Characteristics

Instructions for mock results data entry

- Presenters complete some fields prior to training

- Other fields are blank for attendees to enter data

Screenshot of all completed fields (answer key)
Results Training PRS Test

<table>
<thead>
<tr>
<th>Results Section</th>
<th>Baseline Measure</th>
<th>Add Baseline Measure</th>
<th>Help</th>
<th>Definitions</th>
<th>Descriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Call</td>
<td>Arm/Group Title</td>
<td>Arm/Group Description</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Trainees With Standard of Care</td>
<td>Placebo With Standard of Care</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Baseline Analysis Population Description</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Overall Number of Baseline Participants

<table>
<thead>
<tr>
<th>Test</th>
<th>Trainees enter missing data</th>
<th>Presenters complete other data fields prior to training</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results Training Mock Results

Study Results

Participant Flow

Baseline Characteristics

- Number of Participants [with participants]: 6
- Age (years)
  - Mean (Standard Error): 34.78 ± 9.72
  - Median: 15.54 ± 9.17
- Gender: Male/Female
  - Male: 5
  - Female: 1
- Region of Enrollment: United States: 6

Outcome Measures

- Primary Outcome Measure
- Measure Description: Improved pain assessed using the Visual Analog Scale (VAS) from baseline to 30 minutes

Safety Issues

- Number of Participants with events: 5

Adverse Events

- No adverse events

Limitations and Caveats

- Limitations: few participants, small number of adverse events reported
- Technical problems with measurement leading to uninterpretable data

More Information

- Contact Information: Christine Caffel
- Sponsor: Indiana University

INDIANACTS! Clinical and Translational Science Institute

INFORMATION PRESIDENT FOR RESEARCH
Office of the Vice President for Research
Training and Education

Evaluations for hands-on training:

- **78%** = Never Used or Beginner experience level
- **100%** = Will be able to navigate PRS after training
- **100%** = Interactive and hands-on format was helpful

Training and Education: Lessons Learned

- Key is providing training when users need it
  - Timing
  - Access
- Targeting appropriate audience
  - Research coordinators targeted in the past
  - PIs often delegate compliance tasks to coordinators

🌟 Next steps: offer PRS training online and target investigators
Collaboration: Conclusion

- A decentralized institutional structure offers challenges, but collaboration begins to mitigate those challenges.
- Collaboration is an attempt to promote culture of compliance by addressing many facets of CT.gov.

Review

- Current Events
- Compliance Environment
  - FDAAA
- Compliance Program
  - IU
- Registration Process
- Monitoring Process
- Other Processes
  - PI/RP Departure
- Governance
- Collaboration: Institutional Structure and Elements of an Effective Compliance Program
  - Communication
  - Training and Education
Questions?
Discussion?