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Introduction

ClinicalTrials.gov (CT.gov) is a public registry aimed at increased transparency and improved public awareness of research. Information about individual clinical trials is added to CT.gov through a registration process. Various regulatory bodies and committees have promoted both definitions of those clinical trials required to register and the necessity of results reporting. Indiana University (IU) has both a policy and compliance program that aims to assist the research community with obligations and mitigate risks associated with noncompliance. IU continuously evaluates the regulatory environment with regards to CT.gov requirements and updates both the policy and compliance program as necessary.

Section I – Requirements and Recommendations

A. FDAAA 801 Requirements

The Food and Drug Administration Amendments Act of 2007 (FDAAA 801) provides a definition of clinical trials required to register and provide results in a public registry. Violations can result in an initial $10,000 penalty and up to $10,000 penalty per day for the duration of an uncorrected violation[1]. Additional penalties can include withholding of funds and sanctions.

Per FDAAA 801, Applicable Clinical Trials (ACTs) requiring registration and maintenance on a public registry typically include:

- Drug – a controlled, clinical investigation, other than a phase I clinical investigation, of a drug subject to section 505 of the Federal Food, Drug, and Cosmetic Act or to section 351 of the Public Health Service Act, where 'clinical investigation' has the meaning given in 21 CFR 312.3 (or any successor regulation) and 'Phase I' has the meaning given in 21 CFR 312.21 (or any successor regulation)[1, 6].
- Device – a prospective clinical study of health outcomes comparing an intervention with a device subject to section 510(k), 515, or 520(m) of the Federal Food, Drug, and Cosmetic Act against a control in human subjects (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); and a pediatric postmarket surveillance of a device as required under section 522 of the Federal Food, Drug, and Cosmetic Act[1, 6].

Timeline for entering clinical trials into a public registry is 21 days after the enrolment of the first subject[1].

FDAAA 801 specifies required data elements for registration, maintenance and necessitates results reporting for ACTs when the FDA-regulated drug, biological product or device being evaluated is approved, licensed or cleared[1]. Clinical trials completed prior to December 26, 2007 may not be required to comply with the requirements identified in FDAAA 801[1].

ACTs started on or after March 7, 2012 are required to include a word-for-word statement regarding CT.gov registration in the Informed Consent documentation[5]. At IU, this statement is generally contained in the Confidentiality section of the Informed Consent documentation.

> *A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.*

B. ICMJE Publication Requirements

Differing from the FDAAA 801 requirements, the International Committee of Medical Journal Editors (ICMJE), in 2005, required that all clinical trials be entered into a public registry. Failure to comply with ICMJE requirements can result in an inability to publish with many prominent journals[2].

Clinical trials requiring registration on a public registry typically include:

- Any research project that prospectively assigns people or a group of people to an intervention, with or without concurrent comparison or control groups, to study the cause-and-effect relationship between a health-related intervention and a health outcome[3].

Timeline for entering clinical trials into a public registry is at the time or before enrolment of the first subject[3].

Results reporting is encouraged, but not required[3].

C. CMS Billing Requirements

Originally published by the Centers for Medicare and Medicaid Services (CMS) in January 18, 2008 as a voluntary requirement, as of January 1, 2014, the National Clinical Trial (NCT) number is required for qualified claims. Claims not including the NCT number will not be paid and will be returned for a revision to add the NCT number[4].

Timeline for entering clinical trials into a public registry is prior to submission of a qualified claim[4].

D. NIH Recommendations

For clinical trials receiving funding and/or support from the National Institutes of Health (NIH), the NIH has a definition of clinical trials that are encouraged to register in a public registry. The NIH definition of a clinical trial includes not only those utilizing a prospectively assigned intervention to evaluate biomedical outcomes, but additionally includes those evaluating behavioral outcomes.

Clinical trials that are encouraged to register on a public registry typically include:

- A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

In addition to the clinical trial definition developed by the NIH, usage of the requirements outlined in FDAAA 801 for clinical trials receiving funding and/or support from the NIH is also encouraged.

E. IU Requirements Usage

IU complies with the FDAAA 801 ACT definition regarding those clinical trials requiring registration.

The Office of Research Compliance (ORC) will make a determination if a clinical trial is an ACT and requires compliance with FDAAA 801 requirements.

ICJME requirements may need to be followed in order to publish and it is the responsibility of the Principal Investigator and/or the non-IU sponsor to confirm that requirements for publication are met.

CMS requirements may need to be followed in order to receive payment for qualified claims and it is the responsibility of the Principal Investigator and/or the non-IU sponsor to confirm that requirements for research billing are met.

Responsibility to comply with sponsor specific requirements or non-United States law requiring registration in CT.gov or another public registry is held by the Principal Investigator and/or the non-IU sponsor.

Clinical trials with no European Union sites and requiring registration per FDAAA 801 will use CT.gov as the public registry.

F. Requirements Guide – Table

Regulation/Policy	Timeline for Registration	Results Reporting Required	Penalty for Not Complying
FDAAA 801	21 days post first subject enrollment	Yes	Initial $10,000 and $10,000/day for the duration of the violation (uncorrected violations), withholding of funds, sanctions
ICMJE	At or before first subject enrollment	No	Inability to publish in prominent journals
CMS	Prior to submission of claim	No	Claims will not be paid
NIH	Recommended – 21 days post first subject enrollment	Recommended – Yes	Recommended – not enforced

Section II – Responsible Party Requirements

A. FDAAA 801 Responsible Party Definition

Per FDAAA 801, the party that is required to register the ACT on the public registry is referred to as the Responsible Party and is either the sponsor or a qualified Principal Investigator[1]. The sponsor can delegate responsibility to a qualified Principal Investigator to handle all registration and maintenance in the public registry[1]. A qualified Principal Investigator is an individual who "…is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all the requirements"[1].

B. IU Responsible Party Usage

Due to IU delegation, a Principal Investigator in which the protocol registration has not been completed by the sponsor will be considered the Responsible Party.

The Office of Research Compliance (ORC) can assist in making a determination of the Responsible Party for a clinical trial that is an ACT and requires compliance with FDAAA 801 requirements. Below are sample scenarios and they do not encompass all potential clinical trials.

IND/IDE Clinical Trial, IU Investigator Initiated

Generally, it is the responsibility of the qualified Principal Investigator to complete the protocol registration. Examples include:

- IU investigator holds the IND (Investigational New Drug)/IDE (Investigational Device Exemption) and conducts the study at IU only
- IU investigator holds the IND/IDE and conducts the study at IU and several other sites

IND/IDE Clinical Trial, Not IU Investigator Initiated

Generally, it is the responsibility of the IND/IDE holder (sponsor) to complete the protocol registration. If the sponsor is not completing the protocol registration, the qualified Principal Investigator will become the Responsible Party. Examples include:

- Pharmaceutical company holds the IND/IDE and conducts the study at IU
- Another institution or non-IU investigator holds the IND/IDE and conducts the study at IU and/or other sites

Not IND/IDE Clinical Trial, Externally Funded

Generally, it is the responsibility of the grantee of funds (sponsor) to complete the protocol registration. For these types of clinical trials, IU has delegated the Responsible Party role to the qualified Principal Investigator. Examples include:

- NIH funds are received to conduct a clinical trial without an IND/IDE
- Other federal or non-profit funds are received to conduct a clinical trial without an IND/IDE

Not IND/IDE Clinical Trial, Not Externally Funded

Generally, it is the responsibility of the institution providing support to the Principal Investigator to complete the protocol registration. For these types of clinical trials, IU has delegated the Responsible Party role to the qualified Principal Investigator. Examples include:

- Departmental funds are obtained to conduct a clinical trial without an IND/IDE

C. Responsible Party at IU Guide – Table

IND/IDE Status and Holder	Generally Responsible	If IU Responsible, Delegated to Individual
IND/IDE Clinical Trial, IU Investigator Initiated	Principal Investigator	---
IND/IDE Clinical Trial, Not IU Investigator Initiated	Sponsor (Non-IU IND/IDE Holder)	---
Not IND/IDE Clinical Trial,	Sponsor (IU)	Principal Investigator

Externally & Not Externally Funded*		
*Includes NIH funded protocols Note: Above are sample scenarios and they do not encompass all potential clinical trials		

Section III – Compliance Program Roles and Responsibilities

A. IU Responsibilities

IU is responsible for hosting a compliance program that provides administration, monitoring, auditing, reporting and training for the CT.gov registration and maintenance processes completed by affiliated IU investigators. The ORC is responsible for the compliance program operations.

B. ORC Operational Responsibilities

The ORC depends on the Quality Improvement Office (QIO) to perform the following functions:

- Administer CT.gov accounts
- Assist in determining if a clinical trial is an ACT and requires compliance with FDAAA 801 requirements
- Monitor research community activity and responsibilities within CT.gov
- Monitor compliance program
- Report to executive management on compliance program progress
- Train internal staff and research community on the IU, CT.gov policy and operations
- Handle inquiries/concerns from the research community

C. Research Community Operational Responsibilities

The Research Community, including Principal Investigators determined to be the Responsible Parties of ACTs, performs the following functions:

- Request of account administration needs
- Correctly identify the Responsible Party for a clinical trial requiring action on CT.gov
- Create records on CT.gov
- Approve and release actions associated with CT.gov records
    - Confirm accuracy of content in record
- Resolve problems on CT.gov
- Maintain records on CT.gov including content updates, modification of the verification date and results reporting, if required
- Attend or utilize training
- Notify ORC of receipt of any correspondence from an external agency regarding FDAAA 801 requirements, a CT.gov record, registration requirements or maintenance requirements **within seven days of receipt**
- Notify ORC 30 days prior to an expected and 14 days following an unexpected Principal Investigator/Responsible Party personnel change. If required, complete the modification to the Principal Investigator/Responsible Party in the impacted CT.gov record 30 days prior to an expected and 14 days following an unexpected personnel change or work with ORC in completing a record transfer

Section IV – System Monitoring

A. System Monitoring Purpose

The system monitoring focuses on those protocols and records that have required actions readily identified through CT.gov, Kuali Coeus Institutional Review Board (KC IRB) and the operational lists. These systems and the existing mechanisms are leveraged to determine required actions. The system monitoring focuses on registration, Responsible Party identification, results posting, verification date updates and internal actions within the Human Subjects Office (HSO) and QIO.

B. Research Community Actions in CT.gov

The research community performs several actions within CT.gov that require continuous monitoring through the usage of reports and tracking systems. The monitoring process will focus on FDAAA 801 requirements and other non-FDAAA 801 issues may not be addressed by ORC through monitoring.

The following actions are monitored by QIO:

- Existing and active clinical trial registered on CT.gov (NCT # provided)

  Existing and active clinical trials meeting the ACT requirements need to have a completed registration on CT.gov and have been issued a NCT #[1].

- New clinical trial registered on CT.gov
  - ACT determination

  Clinical trials that meet the ACT definition of a clinical trial require registration on CT.gov[1]. An ACT determination is completed by QIO to determine clinical trials requiring registration on CT.gov.

- IU-sponsored clinical trial identifies Principal Investigator as Responsible Party

  Clinical trials registered with IU as the sponsor are required, per IU policy, to modify the Responsible Party to the qualified Principal Investigator[7].

- Record Verification modified (12 months)

  ACTs that are in an active recruitment status are required to verify the accuracy and if needed, update record content every 12 months[1]. The data element utilized to identify that this check was completed is the Record Verification. At IU, all clinical trials on CT.gov that are in an active record status are requested to verify the accuracy and if needed, update the record content every 12 months.

- Results posted

  ACTs are required to post results 12 months after the Primary Completion date and when the FDA-regulated drug, biological product or device is approved, licensed or cleared by the FDA[1].

- Approve/Release action taken – QIO requested actions

The Responsible Party role must take the Approve/Release action on several modifications made to the record. Actions requested as a part of QIO monitoring are further monitored to confirm that the Approve/Release action is taken by the Responsible Party. Without this action being taken, the modification cannot be reviewed and become a part of the public record.

- Approve/Release action taken – Record Owner requested actions

  The Responsible Party role must take the Approve/Release action on several modifications made to the record. Actions completed by study teams outside of QIO monitoring are monitored to confirm that the Approve/Release action is taken by the Responsible Party. Without this action being taken, the modification cannot be reviewed and become a part of the public record.

- Faculty turnover record reassignment or transfer

  Every record must have a Responsible Party and that Responsible Party should be correctly assigned to the entity or individual that has the ability to perform the functions of the role[1]. In the event that a faculty member leaves the institution, his/her records need to be evaluated to determine if the Responsible Party should be reassigned, if the record should be transferred to the new institution or if the record should have a status change to complete/terminated/withdrawn.

C. HSO Actions in KC IRB

HSO performs several actions within KC IRB including maintenance of the questionnaire and document content that require continuous monitoring through the usage of reports.

The following actions are monitored by QIO:

- KC IRB, CT.gov questionnaire

  The KC IRB, CT.gov questionnaire needs to include accurate selection of the ACT definition and accurate NCT #s when available.

- Informed Consent documentation

  Informed Consent documentation for ACTs started on or after March 7, 2012 is required to include a word-for-word statement regarding CT.gov registration[5].

D. QIO Actions in Compliance Program

QIO performs several actions during the compliance program processes that require continuous monitoring through the usage of reports and tracking systems.

The following actions are monitored by QIO:

- Sending notifications

Timely sending of notifications is essential to enacting the tasks specified in the IU, CT.gov Compliance plan.

- Response to inquiries
  - ACT determination assistance
  - Responsible Party determination assistance
  - New account registration
  - Protocol Registration and Results System (PRS) system assistance
  - Approve and release actions
  - General program assistance

Timely response to inquiries is essential to providing the support needed by the research community and HSO in completing the modifications requested.

E. Monitoring Schedule – Table

Action Originator Area	Function/Responsibility	Frequency of Monitoring
Research Community	Existing and active clinical trial registered on CT.gov (NCT # provided)	Every record as in queue
Research Community	New clinical trial registered on CT.gov • ACT determination	1+ definitions indicated
Research Community	IU-sponsored clinical trial identifies Principal Investigator as Responsible Party	Every record as in queue
Research Community	Record Verification modified (12 months)	Every record/month
Research Community	Results posted	Every record/month
Research Community	Approve/Release action taken – QIO requested actions	Every record/month
Research Community	Approve/Release action taken – Record Owner requested actions	Every record/month
Research Community	Faculty turnover record reassignment or transfer	Every departing faculty member as in queue/month
HSO	KC IRB, CT.gov questionnaire	1+ definitions indicated
HSO	Informed Consent documentation	1+ definitions indicated
QIO	Sending notifications	Every record/month
QIO	Response to inquiries	Every record/month

Section V – Record and Protocol Auditing

A. Record and Protocol Auditing Purpose

The record and protocol auditing focuses on those protocols and records that are not typically captured during the system monitoring tasks. A risk assessment is utilized to determine the records and protocols that should be audited to determine if the trial is applicable to FDAAA 801 and should have been registered in CT.gov. The risk assessment will additionally determine those protocols and corresponding records that had a recruitment status, completion date or content modification that should be reflected

on CT.gov. Data elements from CT.gov, KC IRB and the operational lists will be utilized to identify the auditing pool.

B. Research Community Risk

The research community has several compliance obligations in CT.gov that require continuous auditing through the usage of reports and tracking systems. The auditing process will focus on FDAAA 801 requirements and other non-FDAAA 801 issues may not be addressed by ORC through auditing.

The following actions are audited by QIO:

- Existing and active clinical trial registered on CT.gov (NCT # NOT provided)
    - ACT determination

      Existing and active clinical trials meeting the ACT requirements need to have a completed registration on ClinicalTrials.gov and have been issued a NCT #[1]. An ACT determination is completed by QIO to determine clinical trials requiring registration on CT.gov.

- Results posted
    - ACT determination

      ACTs are required to post results 12 months after the Primary Completion date and when the FDA-regulated drug, biological product or device being evaluated is approved, licensed or cleared[1]. An ACT determination is completed by QIO to determine applicability to FDAAA 801.

- Recruitment status updates
    - ACT determination

      ACTs are required to update record content 30 days following a change[1]. An ACT determination is completed by QIO to determine applicability to FDAAA 801.

- Completion date updates
    - ACT determination

      ACTs are required to update record content 30 days following a change[1]. An ACT determination is completed by QIO to determine applicability to FDAAA 801.

- Content updates
    - ACT determination

      ACTs are required to update record content 12 months following a change[1]. An ACT determination is completed by QIO to determine applicability to FDAAA 801.

C. Record and Protocol Auditing Schedule – Table

Action Originator Area	Function/Responsibility	Frequency of Auditing
Research Community	Existing and active clinical trial registered on CT.gov (NCT # NOT provided) • ACT determination	Risk assessment/quarter *Selected protocols evaluated*
Research Community	Results posted • ACT determination	Risk assessment/quarter *Selected protocols/records evaluated*
Research Community	Recruitment status updates • ACT determination	Risk assessment/quarter *Selected protocols/records evaluated*
Research Community	Completion date updates • ACT determination	Risk assessment/quarter *Selected protocols/records evaluated*
Research Community	Content updates • ACT determination	Risk assessment/quarter *Selected protocols/records evaluated*

D. Risk Assessment – Table

Existing and active clinical trial registered on CT.gov (NCT # NOT provided)		
Question/Data Type	**Question/Data Name(s)**	**Desired Responses**
Protocol Level	Protocol Type	• Full Board
Protocol Level	Protocol Status	• Active – Open to Enrollment • Active – Closed to Enrollment • Active – Data Analysis Only
Funding	Funding Source Type	• Federal • Foundations • Higher Education • Institutional Proposal • Non-Profit • Other • Other Governmental • State of Indiana • Unfunded • Unit • University Internal
FDA Regulated – IND or IDE # protocol and/or Y response to 1 or more questions	FDA IND or IDE #	• IND or IDE # provided
	IU/Investigator Held IND/IDE	• Y
	Does this research involve a drug, biological product, or device for which at least some aspect of the drug's or device's administration or use is dictated by the protocol?	• Y
	Will data be submitted to the FDA?	• Y
	Custom Data – FDA	• Y

Study Phase	Custom Data – Phase I Trial	• N or blank
Clinical Trial Registration	This research project meets the following definitions (check all that apply).	• None of the above
Results posted		
Question/Data Type	**Question/Data Name(s)**	**Desired Responses**
CT.gov Incomplete Results Due Indicator	Primary Completion date	• 12+ months ago
	Results Status	• Blank • In Progress • Released
Protocol Level	Protocol Type	• Full Board
Protocol Level	Protocol Status	• Active – Open to Enrollment • Active – Closed to Enrollment • Active – Data Analysis Only
FDA Regulated – IND or IDE # protocol and/or Y response to 1 or more questions	FDA IND or IDE #	• IND or IDE # provided
	IU/Investigator Held IND/IDE	• Y
	Does this research involve a drug, biological product, or device for which at least some aspect of the drug's or device's administration or use is dictated by the protocol?	• Y
	Will data be submitted to the FDA?	• Y
	Custom Data – FDA	• Y
Study Phase	Custom Data – Phase I Trial	• N or blank
Clinical Trial Registration	This research project meets the following definitions (check all that apply).	• FDAAA
Recruitment status updates, Completion date updates, Content updates		
Question/Data Type	**Question/Data Name(s)**	**Desired Responses**
Protocol Level	Protocol Type	• Full Board
Protocol Level	Protocol Status	• Active – Open to Enrollment • Active – Closed to Enrollment • Active – Data Analysis Only
Study Status Change	Closed to Enrollment Date	• Date within last quarter
	Data Analysis Only Date	• Date within last quarter
	Closed by Investigator Date	• Date within late quarter
Registration Completed and the Responsible Party is IU Affiliated	NCT # Responsible Party	• NCT # provided • IU OR Principal Investigator

Section VI – Compliance Program Response Plans and Communication

A. Research Community Response Plan – CT.gov Actions/Issues

The study team will be sent an email containing the action/issue description, a due date, available resources and contacts. A total of four emails will be sent and the action/issue can be moved to the discipline and enforcement process. Emails will be sent on a schedule and include staff involved in the monitoring, auditing, enforcement and discipline processes.

B. HSO Response Plan – KC IRB Actions/Issues

The HSO screener assigned to the department conducting the research will be included in the final correspondence identifying the actions that need to be completed in correcting the KC IRB, CT.gov questionnaire and/or the Informed Consent documentation. If the KC IRB, CT.gov questionnaire modifications cannot be completed during the HSO review process, those modifications are requested to be completed at the time of the next amendment or continuing review submission to the IRB. Informed Consent documentation modifications are requested as soon as feasible for the study team. The HSO screener may conduct further follow-up with the study team to confirm completion of the required modifications.

C. QIO Response Plan – Operational Actions/Issues

The QIO staff member that performed the error will be sent an email containing the issue description and a due date. One email will be sent followed by a meeting request to discuss resolution. A meeting request may be sent simultaneously with the email if the staff has continuous issues in this operational task. The email and the meeting request will be sent on a schedule and include staff involved in the monitoring and auditing processes.

D. Response Plan – Table

Action Originator Area	Action	Persons Included	Sending Schedule	Due Date
Research Community	1st Email	• Study Team • CTSI RKS Program Manager* (Late Results) • 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* (Late Results) • 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* • Business Manager (Late Results) • Department/Division Chair (Late Results) • Clinical Affairs AVP (Late Results)	2 Weeks Post 1st Email 3 Months Post 1st Email (Late Results)	Due
Research Community	4th Email	• Study Team • 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	At Issue Identification	1 Week
QIO	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, included persons 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.

E. Research Community Reporting

A member of the research community can report a potential concern by contacting QIO directly at 317-274-2123, **ctgov@IU.edu** or through the confidential IU Anonymous Reporting Hotline at **1-888-236-7542**. The IU Anonymous Reporting Hotline can be used to report a potential concern with confidence and without fear of retribution.

F. External Agency Letter Notification

A member of the research community must notify ORC of receipt of any correspondence from an external agency regarding FDAAA 801 requirements, a CT.gov record, registration requirements or maintenance requirements **within seven days of receipt**.

G. Principal Investigator/Responsible Party Change Notification and Modification

In the event the Principal Investigator acting as the Responsible Party on a CT.gov record leaves the institution, is no longer involved with the clinical trial, becomes incapacitated or dies, a notification needs to be sent to ORC and a modification to the impacted CT.gov record may need to occur.

Expected Principal Investigator/Responsible Party Personnel Change

- Notify ORC 30 days prior to an expected Principal Investigator/Responsible Party personnel change
- If the trial is active, complete the modification to the Principal Investigator/Responsible Party, modify the record to reflect the current clinical trial information and notify the newly assigned Principal Investigator/Responsible Party of responsibilities 30 days prior to an expected personnel change
    - If the clinical trial is a candidate for a record transfer, work with ORC to discuss a PRS record transfer and assist with the record transfer process during the 30 days prior to an expected personnel change
- If the trial is not continuing, mark the record as completed/terminated/withdrawn and modify the record to reflect the current clinical trial information 30 days prior to an expected personnel change
    - In the event of a record that is given this status, but requires results, a modification to the Principal Investigator/Responsible Party or record transfer is still required

Unexpected Principal Investigator/Responsible Party Personnel Change

- Notify ORC 14 days following an unexpected Principal Investigator/Responsible Party personnel change
- If the trial is active, complete the modification to the Principal Investigator/Responsible Party, modify the record to reflect the current clinical trial information and notify the newly assigned Principal Investigator/Responsible Party of responsibilities 14 days following an unexpected personnel change
    - If the clinical trial is a candidate for a record transfer, work with ORC to discuss a PRS record transfer and assist with the record transfer process during the 14 days following an unexpected personnel change
- If the trial is not continuing, mark the record as completed/terminated/withdrawn and modify the record to reflect the current clinical trial information 14 days following an unexpected personnel change
    - In the event of a record that is given this status, but requires results, a modification to the Principal Investigator/Responsible Party or record transfer is still required

H. Record Transfer

IND/IDE Clinical Trial, IU Investigator-Initiated

The existing IND/IDE holder maintains the Responsible Party role unless the IND/IDE is transferred to a new Principal Investigator at IU. In the event where the IU Principal Investigator transitions to another institution and continues to hold the IND/IDE, the Responsible Party role for the record will maintain and the record will be transferred to the new institution.

A closed research project in a complete/terminated/withdrawn status that does not require posting of results does not require an update to the Responsible Party or need to be transferred to the new institution.

A closed research project in a complete/terminated status that does require posting of results will require an update to the Responsible Party or need to be transferred to the new institution.

Not IND/IDE Clinical Trial, Externally Funded

An active research project that remains at IU will have the Responsible Party role assigned to a new IU Principal Investigator. An active research project that will continue to be conducted at the new institution will be transferred to the new institution if the new institution becomes the recipient of the external funds. If the active research project continues to be conducted at the new institution but the external funds remain at IU, a new IU Principal Investigator will need to be identified as the Responsible Party if the qualifications for the Responsible Party are met[1].

A closed research project in a complete/terminated/withdrawn status that does not require posting of results does not require an update to the Responsible Party or need to be transferred to the new institution.

A closed research project in a complete/terminated status that does require posting of results will require an update to the Responsible Party or need to be transferred to the new institution.

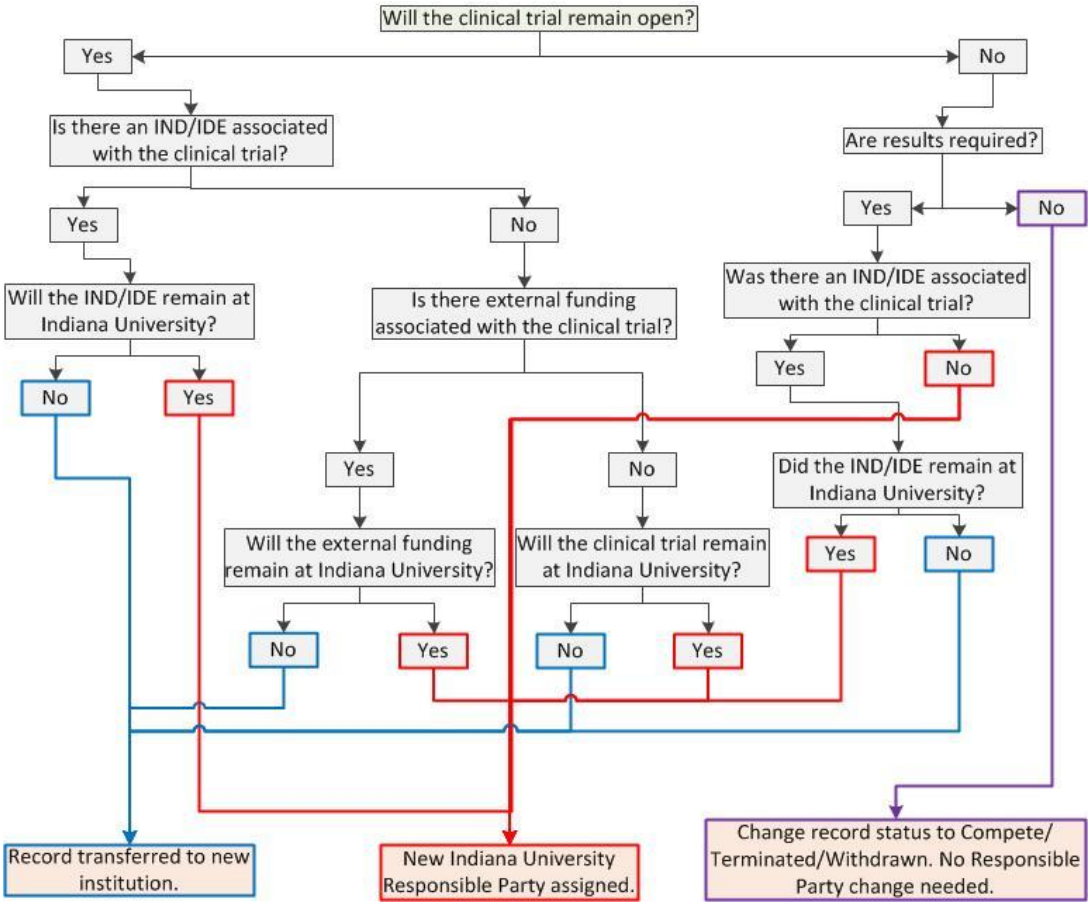
Not IND/IDE Clinical Trial, Not Externally Funded

An active research project that remains at IU will have the Responsible Party role assigned to a new, IU Principal Investigator. An active research project that will continue to be conducted at the new institution will be transferred to the new institution.

A closed research project in a complete/terminated/withdrawn status that does not require posting of results does not require an update to the Responsible Party or need to be transferred to the new institution.

A closed research project in a complete/terminated status that does require posting of results will require an update to the Responsible Party or need to be transferred to the new institution.

I. Record Transfer – Flow



J. PRS Administrator Modifications

For records created more than 12 months ago, but never released, ORC has the option to delete the record.

When a clinical trial has a closed status with the IRB and the study team is unresponsive after completing the notification process, ORC has the option to make administrative updates to the record.

Section VII – Compliance Program Corrective Action, Enforcement and Discipline

A. Clinical Affairs Associate Vice President (AVP) Role

Research Community actions/issues that are not resolved may be sent to the Clinical Affairs AVP through email. The Clinical Affairs AVP will be responsible for the process of resolution and the associated administrative support needed to perform this function. ORC can be requested to additionally support corrective action efforts on an as-needed basis by the Clinical Affairs AVP.

Many of the requirements for registration and maintenance are required by law and violations may additionally be subject to monetary penalties, withholding of funds and sanctions.

Section VIII – Compliance Program Committee Review

A. Committee Objective

A committee is utilized to review the regulatory environment, identify needed operational modifications to address emerging university needs and evaluate the compliance program progress. The committee will meet twice a year and be presented all relevant data and updates needed to perform its functions. The committee is not a decision making body, but instead serves an advisory role.

B. Committee Membership

The committee will be comprised of members selected from the following internal and external stake holders:

- ORC Leadership
- HSO Leadership
- Clinical Trials Contracting (CTC) and/or Clinical Trials Office (CTO) Leadership
- Clinical and Translational Sciences Institute (CTSI) Regulatory and System Expertise
- Research Community Representation

The number of members comprising the committee and the term duration is not mandated.

Section IX – Reporting on Compliance Program

A. Report Content

A report will be distributed to ORC leadership, the committee and the research community and content will differ depending on the audience.

Content will broadly include the following data elements and measures:

- Total ACT determinations completed
- Total new record registrations processed
- Total results reporting monitoring tasks completed
- Total maintenance monitoring tasks completed
- Total trainings completed
- Total registration actions/issues sent to Clinical Affairs
- Total monitoring actions/issues sent to Clinical Affairs

B. Report Distribution

A report identifying compliance program progress will be distributed to ORC leadership on a quarterly basis and distributed to the committee on a semi-annual basis.

Section X – Resources

A. Applicable Regulations, Policies & Guides

Purpose	Access
[1]FDA, FDAAA, Title VIII, Section 801	http://www.gpo.gov/fdsys/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf
[2]ICMJE, "Clinical Trials Registration: A Statement from the International Committee of Medical Journal Editors", September 2004	http://www.icmje.org/news-and-editorials/clin_trial_sep2004.pdf
[3]ICMJE, "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals", December 2015	http://www.icmje.org/icmje-recommendations.pdf
[4]CMS, "Pub 100-04 Medicare Claims Processing: Transmittal 2955"	http://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/downloads/R2955CP.pdf
[5]FDA, 21 CFR § 50.25(c)	http://www.gpo.gov/fdsys/pkg/CFR-2012-title21-vol1/pdf/CFR-2012-title21-vol1-sec50-25.pdf
[6]NIH, "Elaboration of Definitions of Responsible Party and Applicable Clinical Trial"	http://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf
[7]IU, "IU ClinicalTrials.gov: Policy Statement"	http://policies.iu.edu/policies/categories/research/IU-Research-Policies/clinicaltrials.gov.shtml
CT.gov Main Site	http://clinicaltrials.gov/
CT.gov PRS Log-in Site	https://register.clinicaltrials.gov/
CT.gov Researchers Help Site	http://clinicaltrials.gov/ct2/help/for-researcher
FDAAA 801 Required Data Element Definitions	http://prsinfo.clinicaltrials.gov/definitions.html
Identifying an ACT under FDAAA/NIH Flow Chart	http://grants.nih.gov/ClinicalTrials_fdaaa/docs/Flow_chart-ACT_only.pdf
Identifying the Responsible Party under FDAAA/NIH Flow Chart	http://www.grants.nih.gov/ClinicalTrials_fdaaa/docs/registration_flow_chart.pdf
FDA, Informed Consent Guidance	http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM291085.pdf
IU, CT.gov Compliance Program Site	http://researchcompliance.iu.edu/qio/qio_ctgov.html
IU, CT.gov Administrator Email Address	ctgov@iu.edu

B. Acronyms Utilized

Acronym	Definition
ACT	Applicable Clinical Trial
AD	Associate Director
AVP	Assistant or Associate Vice President
CMS	Centers for Medicare and Medicaid Services
CT.gov	ClinicalTrials.gov

CTC	Clinical Trials Contracting
CTSI	Clinical and Translational Sciences Institute
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
ICMJE	International Committee of Medical Journal Editors
IDE	Investigational Device Exemption
IND	Investigational New Drug Application
IRB	Institutional Review Board
KC	Kuali Coeus
NCT Number/#	National Clinical Trial Number
ORC	Office of Research Compliance
PRS	Protocol Registration and Results System
QIO	Quality Improvement Office

C. Terms Utilized

Term	Definition
Approve and Release	The act of the Responsible Party to verify record content and then release the record for review
Billing	Refers to the billing of services that are considered research
Claims/Qualified Claims	Billing documentation sent to CMS requesting reimbursement; qualified claims are those that can seek reimbursement from CMS
Compliance Program	Program that meets established requirements for effectively administering, monitoring, auditing, reporting and training on compliance activity
Investigator Initiated	Refers to clinical trials that involve an investigator held Investigational New Drug (IND) or Investigational Device Exemption (IDE)
Maintenance	The act of continuing to confirm accuracy, update content when needed, address problems when needed and update the verification date in CT.gov
Principal Investigator	Person that is identified as the Principal Investigator on a protocol per IU IRB policies
Problems	Issues that arise during and post the creation of content within records in CT.gov; some problems may require immediate resolution prior to taking additional actions in CT.gov
Protocol	For this purpose, a human subjects research proposal reviewed by the IRB
Public Registry	Refers to a site where the public can view information about clinical trials with the aim to increase transparency and public awareness of research
Registration	The act of creating and completing a record in CT.gov
Results Reporting	Refers to the activity of providing information about findings at the conclusion (primary completion date) of the clinical trial
Sponsor	Organization providing or in some cases receiving financial

	support for the research proposed and conducted
Subject	An individual that is participating in research
Transfer	The process of moving a CT.gov record to another organizational PRS account for management
Verification Date	Movable date within CT.gov that serves as a confirmation that the record has been reviewed by the Responsible Party