THE OHIO STATE UNIVERSITY
COLLEGE OF MEDICINE

Standard Operating Procedure 1
ClinicalTrials.gov Compliance

BACKGROUND

The College of Medicine Office of Research (COMOR) is committed to maintaining an effective, and robust research compliance program. An important component is monitoring College of Medicine (COM) compliance with ClinicalTrials.gov requirements.

ClinicalTrials.gov is a National Institutes of Health (NIH) nationwide registry of clinical trials consisting of an online database for clinicians, researchers, and patients, of publicly and privately funded human subjects research (HSR) studies on a variety of diseases and conditions. Sponsors or Principal Investigators (PI) are required to provide information and updates about applicable clinical trials (ACT) in accordance with (IAW) Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA 801) and Title 42 Code of Federal Regulations Part 11 (42 CFR 11), Clinical Trials Registration and Results Information Submission.

In 2016, NIH published the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information in NIH Guide Notice NOT-OD-16-149. This establishes the expectation that NIH-funded investigators conducting clinical trials (including those not meeting the regulatory definition of ACT), funded in whole or in part by NIH, are registered and that summary results information is submitted to ClinicalTrials.gov.

The revised (effective July 19, 2018) Federal Policy for the Protection of Human Subjects, also known as the Common Rule, codified at 45 CFR 46, states that for clinical trials (including those not meeting the regulatory definition of ACT) conducted or supported by a federal department or agency, one IRB-approved informed consent form (ICF) will be posted on a publicly available federal website in accordance with (IAW) 45 CFR 46.102(b), 46.116(h). The ICF will be posted on the federal website after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol. While there are two federal websites (ClinicalTrials.gov is one) available for this purpose, COM expects that researchers will adhere to the federal requirement using ClinicalTrials.gov.

Some scientific journals require ClinicalTrials.gov registration and compliance as a condition of publication (including those not meeting the regulatory definition of ACT). For example, the International Committee of Medical Journal Editors (ICMJE) requires

trial registration as a condition of the publication of research results generated by a clinical trial.

PURPOSE

To maintain transparency with university partners and the COM research community by standardizing a process for ensuring that COM PIs are aware of their responsibilities and understand COMOR requirements in relation to ClinicalTrials.gov compliance.

APPLICABILITY

This SOP applies to any COM clinical trial registered in ClinicalTrials.gov.

DEFINTIONS

1. Applicable Clinical Trial (ACT):

1.1 Controlled clinical investigations (other than phase 1 investigations) of any FDA-regulated drug or biological product for any disease or condition

1.2 Certain studies of FDA-regulated medical devices, excluding small clinical trials to determine feasibility and certain clinical trials to test prototype devices, but including FDA-required pediatric post-market surveillances of a device product

2. Clinical Trial (NIH): For purposes of NIH policy, a HSR study in which one or more 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

3. Principal Investigator (PI): An individual with the appropriate scientific and/or scholarly training and expertise to assume direct responsibility for the ethical conduct of a study involving human subjects, providing technical and administrative oversight of the research, and making important study-related decisions

4. Problem Record: A study flagged for errors

5. Public Health Service (PHS) Act (42 USC 282(j)(5)): US federal law that describes the expanded clinical trial registry data bank, including coordination and compliance

6. Record Owner: Primary contact for study record

7. Responsible Party: The entity or individual (Sponsor, Sponsor-Investigator or PI) responsible for registering an ACT and submitting ACT information to ClinicalTrials.gov

7.1 Sponsor: The entity (e.g., corporation or agency) that initiates the study

7.1.1.1 The Sponsor may designate a PI as the RP if they meet the following requirements:

7.1.1.2 Is responsible for conducting the study

7.1.1.3 Has access to and control over the study data

7.1.1.4 Has the right to publish the results of the study; and

7.1.1.5 Has the ability to meet all requirements for submitting and updating clinical study information

7.2 Principal Investigator: The individual designated as RP by the Sponsor

7.3 Sponsor-Investigator: The individual who both initiates and conducts the study

PROCEDURE

1. Compliance Monitoring and Enforcement

1.1. PIs are responsible for registering their clinical trial on ClinicalTrials.gov when the Sponsor is not assuming responsibility (serving as the RP) for ClinicalTrials.gov record maintenance.

1.2. COMOR Compliance (COMOR-C) will monitor ClinicalTrials.gov compliance and problem records at least twice per calendar year (CY) and at the time of an audit. Monitoring will include review and analysis of Ohio State ACTs listed on the public-facing website, FDAAA TrialsTracker.

1.3 For departments and divisions whose research is not administratively managed by The Ohio State University Comprehensive Cancer Center (OSUCCC) Clinical Trials Office (CTO):

1.3.1 On a quarterly basis, COMOR-C will prepare and distribute a ClinicalTrials.gov compliance dashboard to COM leadership,

including the Dean, with information about compliant and noncompliant records within COM departments and divisions.

1.3.2 COMOR-C will send notifications of noncompliance via email to Record Owners and Responsible Parties (excluding those from departments and divisions under the OSUCCC CTO) during compliance evaluation periods as described in 1.2.

1.3.3 At any point, COMOR-C, may implement a focused problem records initiative to foster compliance. In this case, Record Owners and Responsible Parties will receive a 30-day deadline for addressing required updates and/or queries on problem records. Reminder emails will be sent 14 days, seven (7) days and one (1) day prior to deadline. COMOR-C will adjust this deadline if needed, to account for any delays emanating from the ClinicalTrials.gov Protocol Registration and Results System (PRS) that are beyond the control of Ohio State.

1.3.3.1 Responsible Parties whose problem records remain unresolved by the 30-day deadline will be subject to Ohio State network account deactivation in collaboration with COM Research Technology Services (COMRTS) until problem records are brought into compliance.

1.3.3.2 Record Owners and Responsible Parties will contact COMOR-C at COMResearchCompliance@osumc.edu after problem records have been resolved. Upon confirmation of record compliance, COMOR-C will initiate Ohio State user account reactivation.

1.4 For departments and divisions with research administratively managed by the OSUCCC CTO, the OSUCCC CTO collaborates with COMOR-C to share ClinicalTrials.gov records information twice per CY and as needed.

2. Additional Reporting Requirements, Potential Penalties, and Other Consequences of Noncompliance

2.1 The FDA makes determinations about whether Responsible Parties are complying with legal requirements for submitting information to ClinicalTrials.gov.

2.1.1 When these requirements have not been met, FDA has the authority to take enforcement action. Responsible Parties receiving a *Pre-Notice of Noncompliance*, have not complied with their legal reporting obligations.

2.1.2 Failure to act following receipt of a *Pre-Notice of Noncompliance*, will result in FDA issuing a *Notice of Noncompliance*. The *Notice of Noncompliance* grants the RP 30 days to submit required information. Otherwise, FDA is authorized to seek civil monetary penalties for violations, including additional civil monetary penalties for failure to submit the required information within the 30-day period.

2.1.2.1 *Notices of Noncompliance* are publicized on the FDA's website and information about the noncompliance is posted within the study record on ClinicalTrials.gov.

2.1.3 Any Ohio State RP receiving a *Pre-Notice of Noncompliance, Notice of Noncompliance,* or similar warning letter, is required to immediately notify COMOR-C and provide a copy of the correspondence via email at: COMResearchCompliance@osumc.edu. COMOR-C will internally track these notifications.

2.1.4 In addition to civil money penalties, violations of § 301(jj) of the Federal Food, Drug, and Cosmetic Act (FFDCA) (21 USC 331 (jj)) could result in other regulatory action, such as injunction and/or criminal prosecution.

2.1.5 IAW § 402(j)(5)(A) of the Public Health Service (PHS) Act (42 USC 282(j)(5)(A)), grant or progress report forms for ACTs funded in whole or in part by the US Department of Health and Human Services (HHS), must include a certification that the RP has made all required registration and results submissions. Otherwise, any remaining funding for a grant or funding for a future grant to such grantee will not be released.

2.1.6 IAW § 402(j)(5)(B) of the PHS Act (42 USC 282(j)(5)(B)), at the time of submission of an application under § 505, 515, 520(m), or 351 of the FFDCA, or submission of a report under § 510(k), the application or submission will be accompanied by a certification that all applicable requirements have been

met. Where available, the certification will include the National Clinical Trial control numbers.

2.1.6.1 If there is a failure to submit a certification under § 402(j)(5)(B) of the PHS Act or knowingly submitting a false certification, the applicant or submitter of the relevant submission to FDA would be subject to the potential consequences set forth.

2.1.6.2 If, however, there is a failure to submit required clinical trial information under § 402(j) of the PHS Act or submitting clinical trial information that is false or misleading, the RP (as identified in the ClinicalTrials.gov record for the ACT) would be subject to the potential consequences set forth.

2.2 The expectations for clinical trial registration and results submissions will be included in the terms and conditions of the award for NIH-funded clinical trials. Failure to comply with the terms and conditions of the NIH award may provide a basis for enforcement actions, including termination, consistent with 45 CFR 75.371 and/or other authorities, as appropriate. If the NIH-funded clinical trial is also an ACT, noncompliance with the requirements specified in 42 USC 282(j) and 42 CFR Part 11 may also lead to actions described in 42 CFR 11.66.

2.3 When a PI plans to depart Ohio State, they must update their ClinicalTrials.gov records accordingly as part of their COM offboarding responsibilities. This includes ensuring that the record is in good standing and:

2.3.1 Completing the record; or

2.3.2 Updating the record to reflect transfer to a new PI; or

2.3.3 Transferring the record to the PI's new institution

RESOURCES

1. ClinicalTrials.gov Protocol Registration System (PRS) Administration: register@clinicaltrials.gov

2. ClinicalTrials.gov Questions and Answers (Q&A)

3. College of Medicine Offboarding & Laboratory Closeout Checklist

4. Managing ClinicalTrials.gov

REFERENCES

1. Title 21 United States Code Section 331 (jj), (21 USC § 331 (jj)), Prohibited Acts

2. Title 42 Code of Federal Regulations Part 11 (42 CFR 11), Clinical Trials Registration and Results Information Submission

3. Title 42 United States Code Section 282 (i), and (j) (42 USC § 282 (i)(j)), Data bank of information on clinical trials for drugs for serious or life-threatening diseases and conditions, Expanded clinical trial registry data bank

4. NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information. Notice Number: NOT-OD-16-149. Release Date: September 16, 2016. Effective Date: January 18, 2017

CONTACT

For questions about this SOP, please contact COMOR-C at: COMResearchCompliance@osumc.edu.

APPROVED

DocuSigned by: Lorri A. Fowler B2A006E91E3346F...	DocuSigned by: 969393D36DD64E9...	DocuSigned by: Daisy Lausell 7EF959EA586344E...
Lorri Fowler Executive Director, Office of Research	**Richard Gumina** Associate Dean, Convergent Research	**Daisy Lausell** Senior Director, Research Compliance

DocuSign

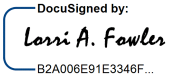
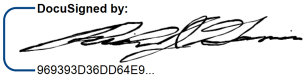
Certificate Of Completion

Envelope Id: 4E15EA48386144AD808E4AFAE6D2BD41
Status: Completed
Subject: Complete with DocuSign: 20221031 CT.gov Compliance SOP 1.pdf
Source Envelope:
Document Pages: 7
Signatures: 3
Certificate Pages: 2
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Enabled
Time Zone: (UTC-05:00) Eastern Time (US & Canada)

Envelope Originator:
Daisy Lausell
1050 Carmack Rd
Columbus, OH 43210
lausell.2@osu.edu
IP Address: 140.254.70.166

Record Tracking

Status: Original
10/29/2022 6:42:37 PM
Holder: Daisy Lausell
lausell.2@osu.edu
Location: DocuSign

Signer Events	Signature	Timestamp
Daisy Lausell lausell.2@osu.edu Senior Director Research Compliance Ohio State University College of Medicine Security Level: Email, Account Authentication (None)	DocuSigned by:  7EF959EA586344E... Signature Adoption: Pre-selected Style Using IP Address: 140.254.70.166	Sent: 10/29/2022 6:51:38 PM Viewed: 10/29/2022 6:51:49 PM Signed: 10/29/2022 6:51:59 PM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		
Lorri A. Fowler fowler.142@osu.edu The Ohio State University Security Level: Email, Account Authentication (None)	DocuSigned by:  B2A006E91E3346F... Signature Adoption: Pre-selected Style Using IP Address: 128.146.207.214	Sent: 10/29/2022 6:51:38 PM Viewed: 11/1/2022 7:49:13 AM Signed: 11/1/2022 7:49:18 AM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		
Richard J Gumina gumina.1@osu.edu MD, PhD The Ohio State University Security Level: Email, Account Authentication (None)	DocuSigned by:  969393D36DD64E9... Signature Adoption: Drawn on Device Using IP Address: 140.254.70.166	Sent: 10/29/2022 6:51:38 PM Viewed: 11/2/2022 11:38:16 AM Signed: 11/2/2022 11:38:24 AM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	10/29/2022 6:51:38 PM
Certified Delivered	Security Checked	11/2/2022 11:38:16 AM
Signing Complete	Security Checked	11/2/2022 11:38:24 AM
Completed	Security Checked	11/2/2022 11:38:24 AM

Payment Events	Status	Timestamps