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Title:	Clinical Trial Disclosure Ancillary Committee Review	

1. PURPOSE

The purpose of this document is to outline the Clinical Trial Disclosure (CTD) Ancillary Committee review processes and procedures completed by the Office of Research Compliance and Quality Assurance (RCQA) and to assess compliance with required disclosure determination.

2. DEFINITIONS

Billing Task Force — A team that consists of representatives from Office of Research Administration (ORA) that reviews information from a study to determine if there is a possibility of billing to Medicare.

Clinical Trial — A research study[1] in which one or more human subjects[2] are prospectively assigned[3] to one or more interventions[4] (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.[5]

[1]See Common Rule definition of *research* at 45 CFR 46.102(d).

[2]See Common Rule definition of *human subject* at 45 CFR 46.102(f).

[3]The term "*prospectively assigned"* refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.

[4]An *intervention* is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

[5]*Health-related biomedical or behavioral outcome* is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects' biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.

CMS	Centers for Medicaid and Medicare Services
CTD	Clinical Trial Disclosure
CTD Ancillary Committee	Any member of the Clinical Trial Disclosure Compliance Team or any manager from RCQA
DOD	Department of Defense
FDAAA	Food and Drug Administration Amendment Act of 2007
FDAMA	Food and Drug Administration Modernization Act of 1997
HSRO	Human Subject Research Office
ICF	Informed Consent Form
ICJME	International Committee of Journal Medical Editors
IRB	Institutional Review Board
NCT #	National Clinical Trial (NCT) number, another term for the ClinicalTrials.gov registry number unique to each record. The format for the ClinicalTrials.gov registry number is "NCT" followed by an 8-digit number, e.g.: NCT00000419.
NIH	National Institute of Health
ORA	Office of Research Administration
Primary Contact	Designated regulatory contact person listed within the electronic IRB system.
Principal Investigator (PI)	An individual who actually conducts a clinical investigation (i.e. under whose immediate direction the test article is administered or dispensed to a subject)

Primary CTD Ancillary Review Committee	Team members of the Clinical Trial Disclosure Compliance Team
PRS	Protocol Registration and Result Reporting System
QCT	Qualifying Clinical Trial - A qualifying clinical trial (QCT) is a trial that meets the requirements set forth in Clinical Trial Policy (NCD 310.1) by the Center for Medicare and Medicaid Services (CMS). This policy delineates the requirements that a trial must meet to be designated as a QCT.
RCQA	Research Compliance and Quality Assurance
Responsible Party	The term used by FDAAA to designate the entity or individual responsible for the clinical trial and for the submission of clinical trial information. This can mean: • The sponsor of the clinical trial, or • The principal investigator if so designated
Sponsor	A person who initiates, but does not actually conduct, the investigation; that is, the investigational drug or device is administered, dispensed or used under the immediate direction of another individual.
Sponsor-Investigator	An individual who both initiates and conducts a clinical investigation and under whose immediate direction the investigational drug or device is being administered, dispensed or used.
Study Team	Principal Investigator, Sponsor-Investigator, Research Coordinator, Study Coordinator, etc.
University of Miami Applicable Clinical Trial (UMACT)	Any study that meets the criteria as defined in the business rules below: **Business Rule #1 – Legal Requirement (FDAAA. FDAMA, and 42 CFR § 11)** <u>Criteria Group 1.1</u> • Study is interventional and involves a Drug, Device, or Biologic; AND • It is Phase 2-4; AND • Study Start Date is as of September 2007 forward (*not programmed)*; AND • Involves at least 1 U.S. Site; AND • PI is the Sponsor-Investigator <u>Criteria Group 1.2</u> • Study is interventional and involves a Drug, Device, or Biologic; AND • It is Phase 2-4; AND

- Study Start Date is as of September 2007 forward (*not programmed)*; AND
- Involves at least 1 U.S. Site; AND
- PI is the Responsible Party

Criteria Group 1.3

- Study is interventional and involves a Drug, Device, or Biologic; AND
- Study Start Date is as of September 2007 forward (*not programmed)*; AND
- Involves at least 1 U.S. Site; AND
- Involves a Serious or Life-Threatening Disease
- PI is the Sponsor-Investigator

Criteria Group 1.4

- Study is interventional and involves a Drug, Device, or Biologic; AND
- Study Start Date is as of September 2007 forward (*not programmed)*; AND
- Involves at least 1 U.S. Site; AND
- Involves a Serious or Life-Threatening Disease
- PI is the Responsible Party

Business Rule #2 – Federal Funding Requirement (NIH Policy on the Dissemination of Clinical Trial Information for Federally Funded Studies)

Criteria Group 2.1

- Study is interventional and involves a Drug, Device, or Biologic; AND
- It is Phase 2-4; OR
- Study is interventional and involves Behavioral Interventions, Dietary Changes, Process of Care Changes, Surgical Procedures , or Physical Therapy; AND
- Study Start Date is as of September 2007 forward; AND
- Involves at least 1 U.S. Site; AND
- NIH or DOD Funding; AND
- PI is the Responsible Party

Business Rule #3 – CMS Mandate Requirement
Criteria Group 3.1

- Study involves a Drug, Device, or Biologic; OR
- Study involves a Behavior, Dietary Changes, Process of Care Changes, Surgical Procedures, or Physical Therapy; AND
- PI is the Responsible Party; AND
- Clinical Study/Registry/Clinical Trial; AND
- Medicare Billing

Criteria Group 3.2 (Sponsored Studies)

- Study involves a Drug, Device, or Biologic; OR
- Study involves a Behavior, Dietary Changes, Process of Care Changes, Surgical Procedures, or Physical Therapy; AND
- Sponsor/Collaborative Group/Other Institution is responsible party; AND
- Clinical Study/Registry/Clinical Trial; AND
- Medicare Billing

Business Rule #4 – ICMJE Requirement
Criteria Group 4.1

- PI is the Responsible Party; AND
- Interventional clinical trial wanting to Publish

Business Rule #5 – Requirement for Result Reporting
Criteria Group 5.1

- Study is interventional and involves a Drug, Device, or Biologic; AND
- It is Phase 2-4; AND
- Study Start Date is as of September 2007 forward; AND
- Involves 1 U.S. Site; OR Study is a Federally Funded interventional clinical trial

3. RESPONSIBILITY

3.1. **CTD Ancillary Review Committee**

- Review study for CTD determination
- Review study to determine who has regulatory responsibility
- Make CTD determination
- Review ICF for applicable CTD language

- Review Federal grant documentation for dissemination plan
- Review of protocol for ClinicalTrials.gov registration ready data elements

3.2. **PI and/or Study Team**

- Submit study in electronic IRB system
- Register protocol in ClinicalTrials.gov if applicable
- Revise ICF if requested
- Revise protocol if requested

3.3. **Billing Task Force**

- Determine if there is a possibility for Medicare billing

3.4. HSRO Staff Member

- Follow-up on ICF revisions if applicable

3.5. ORA

- Follow-up on grant revisions if applicable

4. PROCEDURE

ID	*Step*	*Description*	*Responsible*	*Timing*
4.1. **Determining if study is a UMACT for new submissions**				
4.1.1.	Create new study in electronic IRB system	Data is entered into smart form in electronic IRB system using the relevant information from the protocol and logistics surrounding the conduct of the study.	PI and/or designated study team member	NA
4.1.2.	Submit study	Study is submitted in electronic IRB system for IRB review.	PI or Designee	NA

ID	Step	Description	Responsible	Timing
4.1.3.	Automated UMACT study notification	The CTD Ancillary Review Committee is notified via email and placement of the study into the Ancillary Reviewer Inbox that the study might meet the criteria for a UMACT. Studies that meet the following criteria are forwarded for review: • Funding Source = Federal • Study Scope = 'Yes' for Drug, Biologic, or Device • Clinical Trial = 'Yes' or if 'No,' behavioral interventions, process of care changes, physical therapy, surgical procedures or dietary interventions is checked • Study involves a drug and is Phase 1 – 4 • AND, Submission is a new study or modified study that meets the criteria	Electronic IRB System	At time of submission
4.1.4.	Initiate CTD Determination	The CTD Ancillary Review Committee will initiate their review and determine if a study submitted meets the criteria for registration in ClinicalTrials.gov as defined by the NIH definition	CTD Ancillary review committee	Within 10 business days of submission. *Final determination can exceed timeline window while awaiting PI and/or study team feedback.*

ID	Step	Description	Responsible	Timing
4.1.5.	Review of study to determine responsible party	The CTD Ancillary Review Committee will review the funding documents, additional information smart form, and the protocol to make the determination of regulatory responsibility for registration of the study on ClinicalTrials.gov.	CTD Ancillary review Committee	At time of CTD Determination. *Final determination can exceed timeline window while awaiting study team feedback.*
4.1.6.	Indicate responsible party	After reviewing all of the applicable documents and information provided on the smart forms at study submission, the CTD Ancillary review committee will indicate on the CTD Ancillary review form the responsible party for the study. Investigator should be selected for all studies in which the University of Miami PI initiated the study or has been designated the regulatory responsibility by a sponsor for the study. This option should also be selected for studies in which the PI or a UM PI is the IND or IDE holder. Sponsor should be selected for all studies in which a non-UM investigator, other institution, cooperative group or industry sponsor has regulatory responsibility for the study.	CTD Ancillary Review Committee	At time of CTD Determination. *Final determination can exceed timeline window while awaiting study team feedback*

ID	Step	Description	Responsible	Timing
4.1.7.	Review of study to determine if study meets UMACT Business Requirements	Review of the study in the electronic IRB system to determine if it meets any of the business rules, indicating that it is a UMACT study.	CTD Ancillary Review Committee	At time of CTD Determination. *Final determination can exceed timeline window while awaiting study team feedback*
4.1.8.	Forward to Billing Task Force for review	If unable to determine if a study meets business rule #3, the details of the study are forwarded to the Billing Task Force for review.	CTD Ancillary Review Committee	Within 3 business days of CTD Ancillary Review Committee review
4.1.9.	Determine if study has the potential for Medicare billing	Billing Task force will review the study and determine if study is a QCT and has item(s) potentially billable to Medicare.	Billing Task Force	Within 10 business days of receiving CTD Ancillary Review Committee request for review
4.1.10.	Notify CTD Ancillary Review Committee of Billing Task Force Decision	Once the determination is made, the Billing Task Force will provide their decision in writing to the CTD Ancillary Review Committee.	Billing Task Force	Within 3 business days of Billing Task Force determination

ID	Step	Description	Responsible	Timing
4.1.11.	Indicate determination and applicable business rule	After reviewing all of the applicable documentation, the CTD Ancillary Review committee will make the determination if the study is 'Recommended,' 'Not Required,' or 'Required.' The CTD Ancillary Review committee will also indicate all business rules that apply to the determination.	CTD Ancillary Review Committee	Within 3 business days of receipt by CTD Ancillary Review Committee of Billing Task Force determination, if applicable
4.1.12.	Review of protocol to determine if it is registration ready	The CTD Ancillary review committee will review the protocol using the 'Registration Ready Protocol Review Checklist' for studies in which the responsible party is the Investigator (UM). See SOP RCQA-710.	CTD Ancillary Review Committee	At time of CTD Determination. *Final determination can exceed timeline window while awaiting study team feedback*

ID	Step	Description	Responsible	Timing
4.1.13.	Indicate if protocol is registration ready	The CTD Ancillary Review Committee will indicate on the CTD Ancillary Review form whether or not the protocol is registration ready for Investigator Initiated studies, or Not Applicable for sponsored studies. Registration ready – the protocol has all of the necessary elements needed to facilitate the registration process on ClinicalTrials.gov. Not Registration ready – the protocol is missing required elements as noted in the 'Registration Ready Protocol Review Checklist.' If this option is selected on the form, choose all of the options that apply.	CTD Ancillary Review Committee	At time of CTD Determination. *Final determination can exceed timeline window while awaiting study team feedback*
4.1.14.	CTD Determination and Exception to timeline	Complete CTD Determination and submit within the electronic IRB system using the electronic CTD Ancillary Review Form. *Refer to "Instructions for Completing CTD Ancillary Review" document* If the primary members of the CTD Ancillary Review Committee are not available, designated team members within RCQA will complete the CTD Review on an as needed basis	CTD Ancillary Review Committee	Upon completion of steps 4.1.1 to 4.1.12 or if exception at time of request

ID	*Step*	*Description*	*Responsible*	*Timing*
4.1.15.	Review of ICF	Confirm that ICF has essential element per 21 CFR § 50.25 (c) if study is an 'Applicable Clinical Trial' If study is not an 'Applicable Clinical Trial,' review if relevant ClinicalTrials.gov language is present. Document step on electronic CTD Ancillary Review form as applicable. **Correct language present** – language within ICF is correct for studies that require either the ACT language or the UMACT language. **Language Requires Modification –** language within ICF requires correction, either the language is missing and should be present, the language is present and should not be present, or the language is incorrect for the type of study. **Language is Not Required**- the ICF does not require CTD language.	CTD Ancillary Review Committee	At time of CTD Determination review
4.1.16.	Notification ICF revision needed	PI/Proxy, Primary Contact, and HSRO team member are notified if modification to ICF language is needed	Electronic IRB system	At time of CTD Determination review

ID	Step	Description	Responsible	Timing
4.1.17.	Review of Dissemination Plan	If study is federally funded, grant application is reviewed to verify that a plan for the dissemination of information is present. Document step on electronic CTD Ancillary Review form	CTD Ancillary Review Committee	At time of CTD Determination review
4.1.18.	Notify Study Team via electronic IRB system of Final Determination	The PI and Primary Contact listed in electronic IRB system receive automated confirmation that their study requires registration on ClinicalTrials.gov. The CTD Ancillary Review Committee has the final authority in deciding whether a protocol must be registered on ClinicalTrials.gov. *Refer to "Notification of required registration," "Notification of recommended registration," or "Notification that NCT number is required."*	CTD Ancillary Review Committee / electronic IRB system	Upon completion of determination
4.1.19.	Register protocol in the PRS	Study registered in the PRS. See SOP RCQA-709	PI and/or study team	Prior to enrollment of the first participant

5. DOCUMENTATION

RCQA will maintain an electronic copy of all data used on the shared drive for a minimum of five years that was used to facilitate making a determination.

For example: S:\RCQA\Clinical Trial Disclosure\CTD Compliance

6. REFERENCES

Clinical Trial Disclosure: Determination and Protocol Registration Policy
Food and Drug Administration Amendment Act Section 801: 2007
Food and Drug Administration Modernization Act Section 113: 1997
42 CFR § 11: Clinical Trial Registration and Result Reporting
NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information
Determination of UMACT Workflow
Identifying Responsible Party Workflow
Review of ICF for CTD Language Workflow
Review of Dissemination Plan Workflow
Instructions for completing CTD Ancillary Review form in electronic IRB system
Notification of required registration
Notification of recommended registration
Notification NCT number is required
Notification that ICF language requires modification
Notification that protocol is not registration ready

7. TEMPLATES/FORMS/TOOLS

University of Miami Clinical Trial Registration and Result Reporting Tool

8. REVISION HISTORY

Effective Date	Revision Date	Author	Description of Changes
26 Oct 2015	20 Oct 2015	Y. Davis	• Clarified grammatical errors throughout the document. • Added the CTD Determination Report to the Template/Forms section of the SOP. • Added section 4.2 'Review of Studies that are UMACT per HSR-P-101' • Change title of SOP to reflect the entire review process.
11 Aug 2017	26 Jun 2017	Y.Davis	• Added exception rules for CTD Ancillary review in section 4.1.9 • Clarification of how PI and study team are notified

Effective Date	Revision Date	Author	Description of Changes
			regarding CTD Determination in section 4.1.11 • Incorporated changes to align with 42 CFR § 11 effective January 18, 2017 in section 2 • Added additional criteria for Rule # 3 to indicate when a sponsored study would need to have an NCT number in section 2 • Deleted UMACT Checklist and added the use of the University of Miami Clinical Trial Registration and Result Reporting Tool in section 7 • Included Workflows to accompany SOP • Built out the responsibility section for SOP consistency in section 3 • Added step for ICF review and Follow-up during CTD Determination in section 4.1.10 and 4.1.11 • Added steps for review and escalation process of federally funded grant for verification of plan to disseminate information in step 4.1.12 and 4.1.13 • Added additional definitions for Clinical Trial, HSRO, ORA, Primary Contact, and QCT • Added Clarification to timeline for CTD Determination • Clarified the business rules to be more specific to clinical trials
09 Jun 2020	29 Apr 2020	Y. Davis	• Added protocol review as a function of the CTD Ancillary review committee

Effective Date	Revision Date	Author	Description of Changes
			• Reordered the steps to be consistent with the CTD Ancillary review form • Added clarity to how the CTD Ancillary review form is to be completed. • Added hyperlinks to the regulations that are used as references • Added notification emails in the reference section that are sent with electronic IRB system. • Revised the policy name in the reference section to correspond to the new title. • Corrected the Ancillary Committee name to CTD Ancillary Review Committee

9. SIGNATURES

Prepared by: Yolanda P. Davis Digitally signed by Yolanda P. Davis Date: 2020.06.09 21:41:11 -04'00' Date: _____

Yolanda P. Davis, BS, CCRP
Clinical Trial Disclosure Manager, RCQA

Approved by: Johanna Stamates Digitally signed by Johanna Stamates Date: 2020.06.11 14:05:02 -04'00' Date: _____

Johanna Stamates, RN, MA, CCRC, CHRC
Executive Director, RCQA