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Title:	General CTD Review Procedures	

1. PURPOSE

The purpose of this document is to describe the review process and procedures, supporting documents, and reports pertaining to the review of studies as it relates to Clinical Trial Disclosure.

2. DEFINITIONS

Applicable Clinical Trial (ACT)	The term used in the Food and Drug Administration Amendments Act (FDAAA) to designate interventional studies of drugs, biologics and devices for which information must be submitted to the Clinical Trial Registry Data Bank. An applicable drug clinical trial is a controlled clinical investigation, other than a phase 1 clinical investigation, of a drug subject to section 505 of the Federal Food, Drug, and Cosmetic Act or to section 351 of FDAAA. An applicable device clinical trial is either: (1) a prospective clinical study of health outcomes comparing an intervention with a device subject to sections 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); or (2) a pediatric post market surveillance of a device as required under section 522 of the Food, Drug, and Cosmetic Act.
CTD	Clinical Trial Disclosure
FDAAA	Food and Drug Administration Amendment Act of 2007
IIT	Investigator Initiated Trials
IRB	Institutional Review Board
IRB7	An electronic IRB solution to facilitate tracking of Human Subject Research
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
Principal Investigator (PI)	An individual, who actually conducts a clinical investigation under whose immediate direction the test article is administered, dispensed or used.
Public	Posted on ClinicalTrials.gov public web site.
RCQA	Office of Research Compliance and Quality Assurance

RCQA ED	Executive Director of the Office of Research Compliance and Quality Assurance
QC	Quality Control
Randomly Selected	An electronic research randomizer tool is used to facilitate the random selection of studies that are to be reviewed
Responsible Party (RP)	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 device or biologic 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, device or biologic is being administered, dispensed or used.
Study Team	Principal Investigator, Sponsor-Investigator, Research Coordinator, Study Coordinator, etc.

3. RESPONSIBILITY

3.1. **CTD Compliance Officer or Designee**

- Creates annual CTD review plan
- Notify PI of upcoming CTD comprehensive review
- Performs CTD review
- Issues CTD compliance review report
- Follow-up on PI responses

3.2. **Executive Director of RCQA**

- Review and approval of Annual CTD Comprehensive Review Plan
- Perform Risk Assessment in collaboration with the CTD Manager

3.3. **PI and Study Team**

- Response to CTD Compliance Review Report
- Resolution of identified issues

4. PROCEDURE

ID	*Step*	*Description*	*Responsible*	*Timeline*
4.1. Selection of Human Subject Research Protocol for Review				

ID	Step	Description	Responsible	Timeline
4.1.1.	CTD Comprehensive Review Plan	Studies are added to the Annual CTD Comprehensive Review Plan and saved in \\MEDFS02\Office-Research-compliance\RCQA\Clinical Trial Disclosure\CTD Compliance	CTD Compliance Officer and Executive Director	Annually before March
4.1.2.	Selecting studies for CTD comprehensive review	Investigator Initiated (IIT) studies are reviewed annually for compliance to the regulations and requirements pertaining to CTD. Studies are randomly selected based on the following criteria: • A percentage of the studies established in the Annual CTD review plan for which results were reported within the past year (a minimum of two studies per year) • A percentage of the active studies established in the Annual CTD review plan that meet 'ACT' requirements and that have been registered • A percentage of Sponsor-Investigator active studies established in the Annual CTD review plan (a minimum of two studies per year) • A percentage of the active studies established in the Annual CTD review plan that meet the 'UMACT' requirements and are not 'ACT' studies	CTD Compliance Officer or designee	Annually before March

ID	***Step***	***Description***	***Responsible***	***Timeline***
4.1.3.	CTD Comprehensive Review Internal Tracking	Each study identified in the Annual CTD Comprehensive Review Plan will receive an internal tracking number The tracking number will be assigned per the following nomenclature: CTDYYYY/Sequential order number For example the first CTD Comprehensive Review completed would receive a tracking number of CTD201601	CTD Compliance Officer or designee	

ID	Step	Description	Responsible	Timing
4.2. **CTD Review Notification**				
4.2.1.	Notify the IO	Notify the IO of a CTD review to be scheduled	CTD Manager or RCQA ED	Within 10 business days of planned notification of RP
4.2.2.	Notification of PI/RP	The PI/RP and study team will be notified by email that their study has been selected to undergo a Comprehensive CTD Review which may include an onsite visit to review the regulatory files. For Sponsor-Investigator studies, arrangements will be made for an onsite visit to review the Sponsor/Sponsor-Investigator's regulatory file. *Refer to PI Notification Template*	CTD Compliance Officer or designee	Within 10 business days of scheduled review

ID	*Step*	*Description*	*Responsible*	*Timing*
4.3. **CTD Review Preparation**				
4.3.1.	Review Preparation	In preparation for the review, the study protocol and all amendments, all versions of the informed consent (s) and any other relevant study documentation found in Velos, eProst and/or IRB7 will be reviewed as per CTD Review Checklist	CTD Compliance Officer or designee	Prior to review
4.3.2.	Federal funding information review	If study is federally funded, grant documentation will be reviewed.	CTD Compliance Officer or designee	Prior to review conduct

ID	*Step*	*Description*	*Responsible*	*Timing*
4.4. **CTD Review Conduct**				
4.4.1.	Comprehensive Review of Protocol Records	A review of the ClinicalTrials.gov record against the supporting documentation in the electronic IRB system (i.e. IRB7) will be completed. As applicable, other supporting documents will be reviewed during the Comprehensive Review (e.g. Clinical Study Reports, Manuscripts, and/or Journal Articles). CTD Review Checklist will be utilized to facilitate the review process.	CTD Compliance Officer or designee	Within 2 business days of scheduled date of review

ID	Step	Description	Responsible	Timing
4.4.2.	Report generation	CTD Compliance Review Report is generated, see SOP RCQA-702	CTD Compliance Officer or designee	Within 10 business days after completion of review
4.4.3.	Issue draft report	The final CTD Compliance Review Report will be forwarded to the PI via email with complete instructions on resolving identified issues.	CTD Compliance Officer or designee	Within 5 business days of generating the report
4.4.4.	CTD Review Meeting	CTD review meeting will take place to discuss the observations noted during the review	Responsible Party, Study Team and CTD Compliance Officer or designee	Within 3 business days of receiving draft report
4.4.5.	RP response	The Responsible Party will review the CTD review report and provide corrective and preventive action (if applicable) to all observations noted	Responsible Party	Within 5 business days of receiving report
4.4.6.	Follow-up	Per the CTD Compliance Review Report Follow-Up activities section, a follow-up review on the issues identified is performed to verify that all required action items have been completed	CTD Compliance Officer or designee	Timeline to be determined by RP response

ID	*Step*	*Description*	*Responsible*	*Timeline*
4.5. Review of Completed Studies				
4.5.1.	Review of study per Annual CTD Review Plan	Study is reviewed as per section 4.1.3 to 4.1.6	CTD Compliance Officer or designee	As per Annual CTD Review Plan
4.5.2.	Risk Analysis of completed Studies that are public	If a study has a status of completed with results publicly available, and discrepancies are identified in fields required by FDAAA 801 or 42 CFR § 11, a risk analysis will be performed to determine if corrections should be made to the record. *(see Risk Determination)*	CTD Compliance Officer and ED of RCQA	Within 7 calendar days of discovering issue(s)
4.5.3.	Notification of Issue	If a discrepancy is considered high risk, the RP and study team listed within the ClinicalTrials.gov record will be notified via email communication with a list of issue (s) identified, associated with the record	CTD Compliance Officer or designee	Within 7 calendar days of Risk Analysis
4.5.4.	Problem Resolution	The RP and/or study team will work with the CTD Team to resolve all issues identified.	Responsible Party or designee	Within 14 calendar days of Notification of Issue(s)

ID	*Step*	*Description*	*Responsible*	*Timeline*
4.5.5.	Continued Review of Compliance Issues of Closed Studies	For studies in which issues have been appropriately resolved, the Study Teams will receive notification that their record is now compliant. -or- For studies in which issues have not been resolved or resolutions are not in progress, the Study Team will receive notification that they are non-compliant.	CTD Compliance officer or designee	Within 60 days of the timeline noted in the RP response
		90 days of continued non-compliance for 'ACT' will be escalated to the Institutional Official and Chief Compliance Officer	CTD Compliance Officer or designee	Within 90 days of continued non-compliance associated with the timeline noted in the RP response

5. DOCUMENTATION

RCQA will maintain an electronic copy

6. REFERENCES

21 CFR § 50.25 (c)
42 CFR § 11
Food and Drug Administration Amendment Act; Section 801; 2007
Food and Drug Administration Modernization Act; Section 110; 1997
Food and Drug Administration Compliance Program Guidance Manual (Form FDA 2438) March 11, 2011
ClinicalTrials.gov_Basic Results_Data Element Definitions (DRAFT)
ClinicalTrials.gov_Data Element Definitions (DRAFT)

SOP RCQA-702 CTD Compliance Report Generation

7. TEMPLATES/FORMS

CTD Comprehensive Review Plan
CTD Compliance Review Report
CTD Compliance Review Follow-up Report
'ACT' Report
PI Notification Template

8. REVISION HISTORY

Effective Date	Revision Date	Author	Description of Changes
18 Apr 2017	18 Apr 2017	Y.Davis	• Changed the title for clarity within the subject header • Edited the purpose in section 1 to clearly state what the scope of the SOP • Incorporated the CTD preparation for review in section 4.3. • Aligned the processes with QA Auditing in section 4.4 • Added reference to 42 CFR § 11 in section 6. • Revised procedures related to review of studies that are closed in section 4.5.

9. SIGNATURES

Prepared by: Signature on File Date: 18 Apr 2017
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Approved by: Signature on File Date: 18 Apr 2017
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