Storage & Archival Of Documents & Data

Module 6 Topic 6

"Essential" Documentation

Documentation, Record Keeping, and Retention

- Permits evaluation of the conduct of a study
- Permits evaluation of data collected
- Demonstrates GCP and compliance with applicable regulatory requirements
- Facilitates study management and oversight
- Allows for monitoring and evaluation of practices

Essential Documents - Regulatory Binder

- Essential Documents must be organized and retained for the conduct of clinical studies.
- These organized documents are referred to as the REGULATORY BINDER
- The binder must be kept at the Investigator's clinical site

**TIP: Synonyms: Investigator Binder = Regulatory Binder = Investigational Site File (ISF) = Study Binder = Master Trial File (MTF)

Regulatory Binder

Purpose

- To provide an organizational framework for filing paper versions of essential study documents (or referencing location of an electronically stored file)
- Compliance for Good Clinical Practice
- Core documentation required by Good Clinical Practices (GCP) before a study is initiated
- Additional GCP-required essential documents satisfy NIH grant documentation requirements
- To ensure all GCP-required essential documents are in place and in order for the clinical trial

Good Clinical Practice (E6) Section 8.1, 8.2, 8.3, 8.4

Regulatory Binder

Essential Study Documents Overview

- Study Protocol – signed, dated by all entities (PI, sponsor)
- Study Protocol Amendments
- Informed Consent
- IRB Approval(s)
- Delegate of Authority and Log of Responsibilities
- Curriculum Vitae (CV's) current
- Financial Disclosures

Regulatory Binder

Essential Study Documents Overview (contd)

- Protocol Training Documentation
- Training Documentation to conduct research, study-related duties or functions
- Adverse Events and/or unanticipated events
- Study Protocol Deviations
- Note to File (NTF)
- Standard Operating Procedures(SOPs); Manual of Procedures (MOPs) and or Appendixes
- All communication s between entities (PI, research team, CRO, sponsors, governing boards)

Protocol & Amendments

- IRB-approved Protocol (original and amendments)
- Signed principal investigator (PI) signature pages (PI address/ signature/date)
- IRB-approved Case Report Forms (CRF's)
- IRB-approved advertisements, brochures, letters
- IRB-approved Participant Information Sheets
- IRB-approved Protocol Amendments and (PI) signature page
- Store in reverse chronological order - current approved version first
- Log of protocol changes

IRB Documentation & Approvals

- IRB contact information for missing documents
- Updated IRB Membership Rooster
- IRB registration
- IRB approval letters
- Original IRB application/New Project Submission
- IRB correspondence related to contingent approvals or stipulations
- IRB interim/annual review progress reports
- HIPAA authorization, waiver, and or research preparation purposes

Informed Consent Documents

- IRB-approved/stamped consent documents (clean copy)
- IRB-approved/stamped assent documents
- IRB-approved/stamped short form consents for non-English languages include guidance for consent of non-English speaking
- Place most currently approved consent in plastic sleeve
- Store in reverse chronological order with current approved version
- Log of Informed Consent versions

Investigator Qualification Documentation

- Current Updated investigator and sub-investigator curriculum vitae (CVs) with address, signature and date
- CVs address should reflect address on 1572
- Current clinical professional licensure (dental, medical, nursing, pharmacy, etc.) for PI and co-investigators, if licensed
- Update CV and licensure documents as they expire
- The CV & licensure dates should reflect mirror each other.

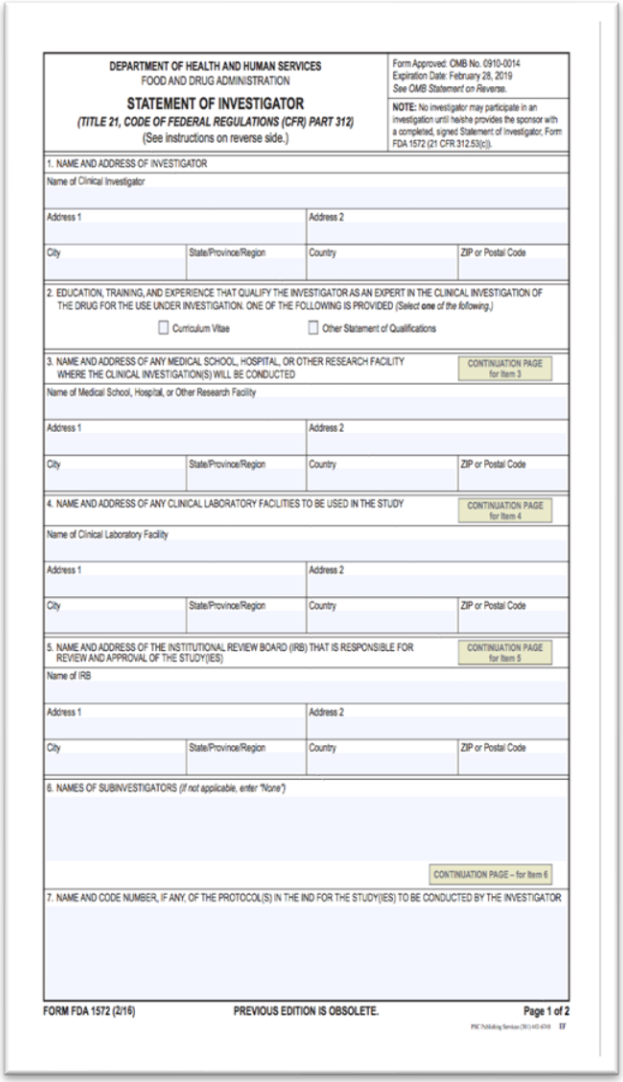
Clinical Investigator's Brochure (IB)

- Clinical investigator's brochure (drug or device) or
- Package insert; include labeling for approved medications
- All amendments to the IB
- Device information sheet/manual

FDA Documents

- FDA Form 1571 (if applicable): Date and sign all versions
- FDA Form 1572 (If applicable): Investigator initiated INDs
- Signed investigator agreement (if applicable)
- Samples of labels attached to investigational product containers
- Regulatory approval or authorization
- FDA Correspondence Log (if applicable)

Example: Form FDA 1572:



DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

STATEMENT OF INVESTIGATOR
(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)
(See instructions on reverse side.)

Form Approved: OMB No. 0910-0014
Expiration Date: February 28, 2019
See OMB Statement on Reverse.

NOTE: No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

1. NAME AND ADDRESS OF INVESTIGATOR

Name of Clinical Investigator

Address 1 | Address 2

City | State/Province/Region | Country | ZIP or Postal Code

2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFY THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS PROVIDED (*Select one of the following.*)

☐ Curriculum Vitae ☐ Other Statement of Qualifications

3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL, OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED — CONTINUATION PAGE for Item 3

Name of Medical School, Hospital, or Other Research Facility

Address 1 | Address 2

City | State/Province/Region | Country | ZIP or Postal Code

4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY — CONTINUATION PAGE for Item 4

Name of Clinical Laboratory Facility

Address 1 | Address 2

City | State/Province/Region | Country | ZIP or Postal Code

5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE STUDY(IES) — CONTINUATION PAGE for Item 5

Name of IRB

Address 1 | Address 2

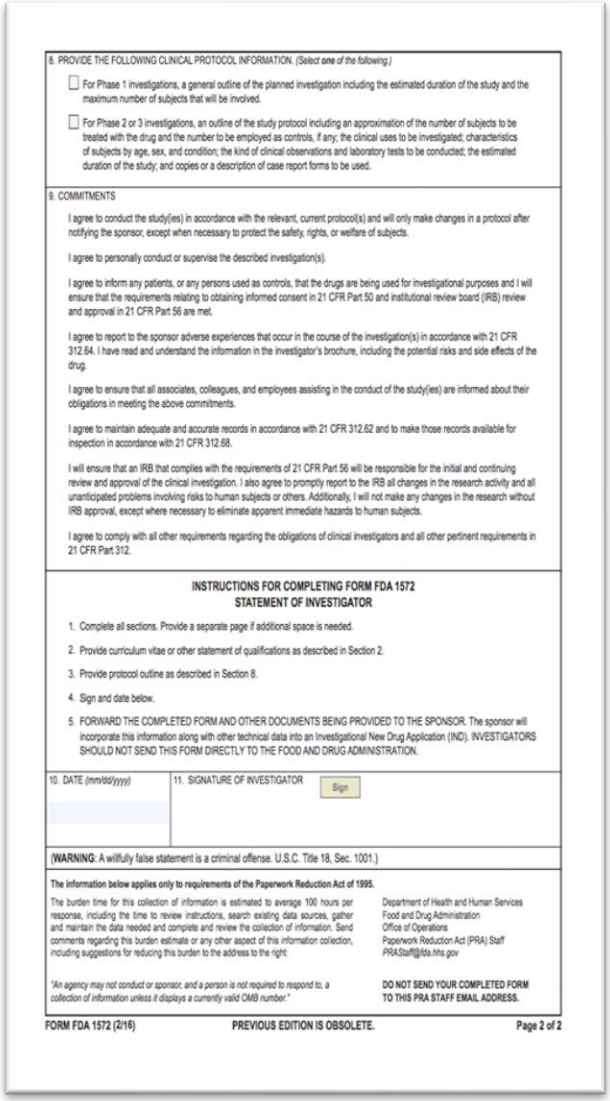
City | State/Province/Region | Country | ZIP or Postal Code

6. NAMES OF SUBINVESTIGATORS (*If not applicable, enter "None"*)

CONTINUATION PAGE – for Item 6

7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR

FORM FDA 1572 (2/16) PREVIOUS EDITION IS OBSOLETE. Page 1 of 2



8. PROVIDE THE FOLLOWING CLINICAL PROTOCOL INFORMATION. (*Select one of the following.*)

☐ For Phase 1 investigations, a general outline of the planned investigation including the estimated duration of the study and the maximum number of subjects that will be involved.

☐ For Phase 2 or 3 investigations, an outline of the study protocol including an approximation of the number of subjects to be treated with the drug and the number to be employed as controls, if any; the clinical uses to be investigated; characteristics of subjects by age, sex, and condition; the kind of clinical observations and laboratory tests to be conducted; the estimated duration of the study; and copies or a description of case report forms to be used.

9. COMMITMENTS

I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects.

I agree to personally conduct or supervise the described investigation(s).

I agree to inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Part 56 are met.

I agree to report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 21 CFR 312.64. I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug.

I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.

INSTRUCTIONS FOR COMPLETING FORM FDA 1572
STATEMENT OF INVESTIGATOR

1. Complete all sections. Provide a separate page if additional space is needed.
2. Provide curriculum vitae or other statement of qualifications as described in Section 2.
3. Provide protocol outline as described in Section 8.
4. Sign and date below.
5. FORWARD THE COMPLETED FORM AND OTHER DOCUMENTS BEING PROVIDED TO THE SPONSOR. The sponsor will incorporate this information along with other technical data into an Investigational New Drug Application (IND). INVESTIGATORS SHOULD NOT SEND THIS FORM DIRECTLY TO THE FOOD AND DRUG ADMINISTRATION.

10. DATE (*mm/dd/yyyy*) | 11. SIGNATURE OF INVESTIGATOR — Sign

(**WARNING**: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

The information below applies only to requirements of the Paperwork Reduction Act of 1995.

The burden time for this collection of information is estimated to average 100 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the address to the right.

Department of Health and Human Services
Food and Drug Administration
Office of Operations
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

DO NOT SEND YOUR COMPLETED FORM TO THIS PRA STAFF EMAIL ADDRESS.

FORM FDA 1572 (2/16) PREVIOUS EDITION IS OBSOLETE. Page 2 of 2

Financial Disclosure Forms (FDF)

- Signed Financial Disclosure Forms for PI, sub-PIs, co-investigators, and applicable research team members
- Update if disclosure changes

Delegation of Authority (DoR) or Responsibilities Log

- Delegation of authority log with role descriptions;
- Involvement start and stop dates; PRINTED name, initials, and original signatures

Example: Delegation of Authority (DoR)

Delegation of Responsibilities Log

Investigator Name:	Protocol:	Site Number:

List staff to whom the Principal Investigator (PI) has delegated significant study-related duties.

Name	Responsibilities*	Initials	Signature	Start Date	End Date	PI Initials/Date

By initialing above, I, the PI, declare that during the conduct of the above study, I have delegated the following study-related activities:

*Responsibilities Legend		
1. Administer Consent	6. Randomize Subjects	11. Complete Study Forms
2. Screen Subjects	7. Dispense Study Drug	12. Provide Discharge Instructions
3. Obtain Medical History	8. Drug Accountability	13. Make Follow-up Phone Calls
4. Perform Physical Exam	9. Assess Adverse Events	14. Query Management
5. Determine Eligibility	10. Complete Source Documents	15.

Signature of Principal Investigator: _____ Date: _____

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Check if final page of log: ☐

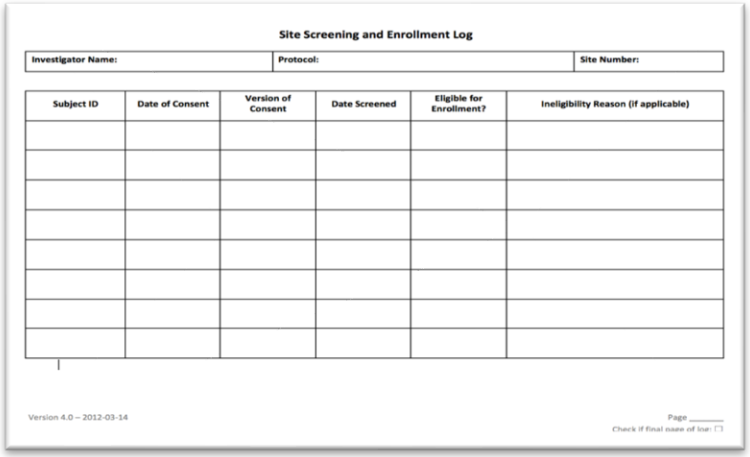
Clinical Research & Study Training

- Documentation of educational completion certificates for Human Subject Protections and Good Clinical Practice training for all staff members (CITI)
- Documentation of study-related training
- Dangerous Goods training (if applicable)
- Documentation of shipping biologics (IATA)
- Procedure training log

**TIPS: Current certifications based on institutional, GCP, & ICH guidelines

Screening/Enrollment

- Subjects who were screened; reasons for screen failure
- Enrollment log
- Site screening plan



Site Screening and Enrollment Log

Investigator Name:	Protocol:	Site Number:

Subject ID	Date of Consent	Version of Consent	Date Screened	Eligible for Enrollment?	Ineligibility Reason (if applicable)

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Page _____

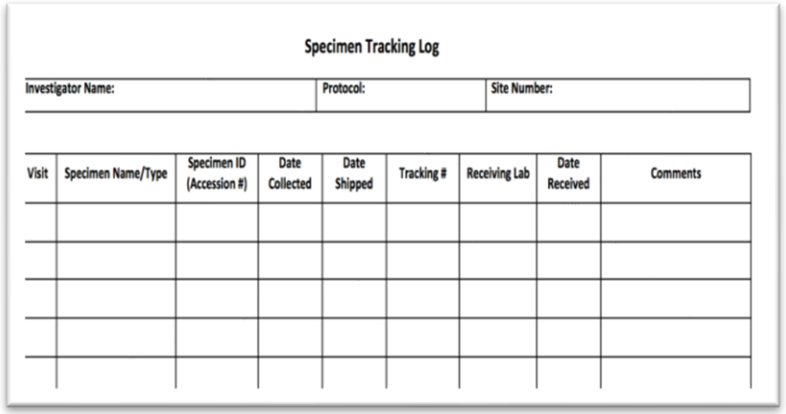
Check if final page of log: ☐

Signed Consent Documents

- All original signed IRB approved and stamped versions consent documents

Subject Visit Tracking Log

- Log all enrolled subject visits
- Reasons for Early Termination (ET)
- Tracks/keeps scheduled visits as per protocol



Specimen Tracking Log

Investigator Name:	Protocol:	Site Number:

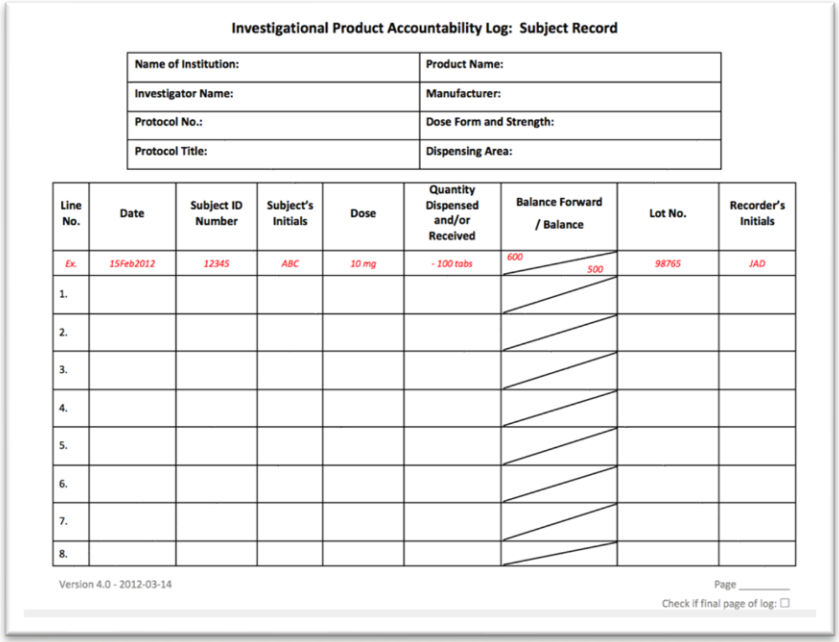
Visit	Specimen Name/Type	Specimen ID (Accession #)	Date Collected	Date Shipped	Tracking #	Receiving Lab	Date Received	Comments

Subject Identification Code List

- Confidential list of subject names
- Link between identity and study code to allow only the
- Investigator to reveal identity of any subject

Study Product Records

- Documentation of study product disposition
- Investigational Product Accountability Log: Stock Record
- Investigational Product Accountability Log: Subject
- Dispense Record



Investigational Product Accountability Log: Subject Record

Name of Institution:	Product Name:
Investigator Name:	Manufacturer:
Protocol No.:	Dose Form and Strength:
Protocol Title:	Dispensing Area:

Line No.	Date	Subject ID Number	Subject's Initials	Dose	Quantity Dispensed and/or Received	Balance Forward / Balance	Lot No.	Recorder's Initials
Ex.	15Feb2012	12345	ABC	10 mg	- 100 tabs	600 / 500	98765	JAD
1.								
2.								
3.								
4.								
5.								
6.								
7.								
8.								

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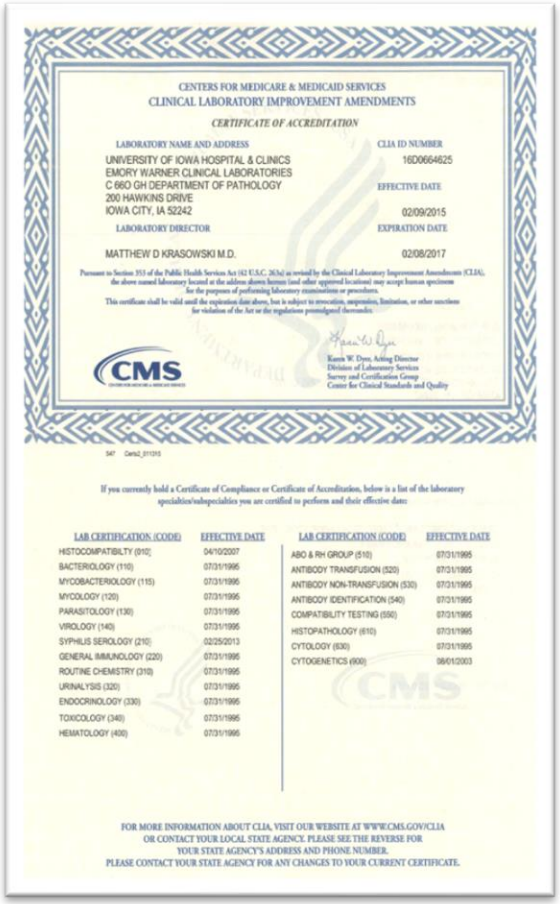
Local Clinical Lab Certificates/ Reference Ranges

- Laboratory reference ranges
- Copy of laboratory certification and accreditations

Lab Specimen Tracking Log

- Specimen sample log
- Shipping documentation
- Storage temperature logs

Local Clinical Lab Certificates



CENTERS FOR MEDICARE & MEDICAID SERVICES
CLINICAL LABORATORY IMPROVEMENT AMENDMENTS
CERTIFICATE OF ACCREDITATION

LABORATORY NAME AND ADDRESS
UNIVERSITY OF IOWA HOSPITAL & CLINICS
EMORY WARNER CLINICAL LABORATORIES
C 660 GH DEPARTMENT OF PATHOLOGY
200 HAWKINS DRIVE
IOWA CITY, IA 52242

CLIA ID NUMBER
16D0664625

EFFECTIVE DATE
02/09/2015

EXPIRATION DATE
02/08/2017

LABORATORY DIRECTOR
MATTHEW D KRASOWSKI M.D.

Pursuant to Section 353 of the Public Health Services Act (42 U.S.C. 263a) as revised by the Clinical Laboratory Improvement Amendments (CLIA), the above named laboratory located at the address shown hereon (and other approved locations) may accept human specimens for the purposes of performing laboratory examinations or procedures.
This certificate shall be valid until the expiration date above, but is subject to revocation, suspension, limitation, or other sanctions for violation of the Act or the regulations promulgated thereunder.

CMS

Karen W. Dyer, Acting Director
Division of Laboratory Services
Survey and Certification Group
Center for Clinical Standards and Quality

If you currently hold a Certificate of Compliance or Certificate of Accreditation, below is a list of the laboratory specialties/subspecialties you are certified to perform and their effective date:

LAB CERTIFICATION (CODE)	EFFECTIVE DATE	LAB CERTIFICATION (CODE)	EFFECTIVE DATE
HISTOCOMPATIBILTY (010)	04/10/2007	ABO & RH GROUP (510)	07/31/1995
BACTERIOLOGY (110)	07/31/1995	ANTIBODY TRANSFUSION (520)	07/31/1995
MYCOBACTERIOLOGY (115)	07/31/1995	ANTIBODY NON-TRANSFUSION (530)	07/31/1995
MYCOLOGY (120)	07/31/1995	ANTIBODY IDENTIFICATION (540)	07/31/1995
PARASITOLOGY (130)	07/31/1995	COMPATIBILITY TESTING (550)	07/31/1995
VIROLOGY (140)	07/31/1995	HISTOPATHOLOGY (610)	07/31/1995
SYPHILIS SEROLOGY (210)	02/25/2013	CYTOLOGY (630)	07/31/1995
GENERAL IMMUNOLOGY (220)	07/31/1995	CYTOGENETICS (600)	08/01/2003
ROUTINE CHEMISTRY (310)	07/31/1995		
URINALYSIS (320)	07/31/1995		
ENDOCRINOLOGY (330)	07/31/1995		
TOXICOLOGY (340)	07/31/1995		
HEMATOLOGY (400)	07/31/1995		

FOR MORE INFORMATION ABOUT CLIA, VISIT OUR WEBSITE AT WWW.CMS.GOV/CLIA
OR CONTACT YOUR LOCAL STATE AGENCY. PLEASE SEE THE REVERSE FOR
YOUR STATE AGENCY'S ADDRESS AND PHONE NUMBER.
PLEASE CONTACT YOUR STATE AGENCY FOR ANY CHANGES TO YOUR CURRENT CERTIFICATE.

COLLEGE of AMERICAN PATHOLOGISTS

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

The College of American Pathologists
certifies that the laboratory named below

University of Iowa Hospitals & Clinics
Emory Warner Clinical Laboratories
Iowa City, Iowa
Matthew D. Krasowski, MD,PhD

CAP Number: 1768801
AU-ID: 1183440
CLIA Number: 16D0664625

has met all applicable standards for accreditation and is hereby accredited by the College of American Pathologists' Laboratory Accreditation Program. Reinspection should occur prior to November 20, 2017 to maintain accreditation.

Accreditation does not automatically survive a change in director, ownership, or location and assumes that all interim requirements are met.

Chair, Commission on Laboratory Accreditation

President, College of American Pathologists

https://www.medicine.uiowa.edu/pathology/research/pathology-clinical-trials-support-core

Serious Adverse Events (SAEs)

- SAE forms or memos
- Correspondence, copies and acknowledgement of reports of internal AEs
- External reports to IRB, Sponsor, regulatory authorities

Unanticipated Problems

- Unanticipated Problems reports to IRB, Sponsor and regulatory authorities

Clinical Site Monitoring Visits

- Monitoring Visit Signature Log
- Each Visit's correspondence
- Post visit follow up letters

Study Communication

- Letter of Understanding/Confidentiality Agreement
- Data Sharing Agreement
- Material transfer Agreement
- Signed agreements between parties (i.e. sponsor/investigators)
- Important decisions regarding study conduct, such as notes to the Study File - Notes to File (NTF)

Guideline for Writing Notes to File (NTF)

Written to identify a discrepancy or problem in the conduct of the clinical research study to note:

- Root cause of the identified problem
- Identify the corrective action taken to prevent recurrence of the problem
- Document that the corrective action has resolved the problem
- The note should be forward-looking and not seek to explain an error discovered
- Print on institution letterhead initiated and authored by an individual responsible for its content

Guideline for Writing Notes to File (contd)

Retention and Distribution:

NTF should be kept on site in the site regulatory file,

Made available to the clinical site monitors reviewing the site's documents and procedures.

If the issue relates to PI responsibilities (e.g., human subject protection, data integrity at the site), the PI should write and sign the note to file.

If the issue relates to actions taken by the sponsor or monitor (e.g., clarification of a protocol section), an appropriate credentialed individual from the sponsor should write and sign the note to file.

Confidentiality & Security

- Filing space should be available for the storage of TMF and local ISF during the conduct of the clinical trial. ISFs will normally be stored in an investigator's office or local filing area
- At the end of the trial the files must be transferred to a suitable archiving facility

Record Keeping

Investigators must ensure that data are recorded and stored correctly and accurately. This not only includes data recorded on Case Report Forms (CRFs) but also all original source data(patient medical notes for example), laboratory test results, radiological images and pharmacy data (drug dispensing records and drug accountability records for example)

Environmental Conditions

- The minimum requirement is for documentation to be stored in conditions that minimize the risk of damage or loss of information
- The risk of damage from water should be reduced by storing documentation above floor level and away from overhead water pipes
- Documentation should be located in areas with minimal variation in temperature and humidity if stored long periods of time