Regulatory Documentation: What do you need in a regulatory binder?

University of Mississippi Medical Center

A Little About Me:

- **Clinical Experience:**
  - Telemetry
  - Neuro Step-Down
  - Neuro Intensive Care
  - Clinical Research
    - Neurology, Geriatric, NICU, and ED
- **Education**
  - Undergraduate- Mississippi College
  - Graduate School- Louisiana State University Health Sciences Center
  - Doctorate Education- University of Mississippi Medical Center
    - BSN to DNP Family Nurse Practitioner Track

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Objectives

Attendees should be able to:

(1) Identify the rationale for regulatory document requirements;

(2) Identify the contents of a regulatory and participant binder;

(3) Identify best practices related to regulatory and other study documentation;

(4) Identify reportable events and required documentation.

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Regulatory Documentation

- **Why Regulatory Documents are required for Clinical Studies and Clinical Trials?**
  - Regulatory documents are submitted to track and evaluate the ethical and procedural conduct of clinical research and the quality of the data that is produced
  - Regulatory documents demonstrate the compliance of the Investigator, Sponsor, and IRB

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Regulatory File Documents Guidelines

- Investigators must maintain a set of records for each study, and all essential documents must be in the file
- Must be established at beginning of each study
- Updated throughout life of study
- Regulatory Guidelines:
  - ICH/GCP at www.ich.org
  - 21 CFR 11, 50, etc. at www.fda.gov
  - 45 CFR 46 at http://ohrp.osophs.dhhs.govwith the standards of Good Clinical Practice and with all applicable regulatory requirements

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Regulatory Binder Set-Up

- Binder set-up may vary based on the study type
  - Clinical Trial
  - Observational Studies
  - Phase I Studies
  - Phase IV Studies
  - Device Studies
- Binder set-up may vary based on the sponsor or Contract Research Organization (CRO) requirements.
- Your site CRA may also have recommendations for binder set-up

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Regulatory Binder Set-Up

- Binder Sections
  - Study Protocol
  - Documents related to the study participant
  - Investigator's Brochure
  - Institutional Review Board (IRB)
  - Monitoring and Site Management
  - Investigator and Study Personnel Documentation
  - Study Medication
  - Laboratory
  - SAE Reporting and Safety
  - Data Management
  - Equipment and Study Materials
  - Correspondence

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Regulatory Binder

- Study Protocol
  - Protocol and Amendments
  - Protocol Clarification Letters
  - Investigator Protocol Signature Pages

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PROTOCOL AMENDMENT ACCEPTANCE FORM

TITLE:	**LONGITUDINAL AMYLOID PET IMAGING SUBSTUDY ASSOCIATED WITH:** *A PHASE III, MULTICENTER, RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP, EFFICACY AND SAFETY STUDY OF GANTENERUMAB* **IN PATIENTS WITH** *EARLY* **(PRODROMAL TO MILD)** *ALZHEIMERS* **DISEASE**
PROTOCOL NUMBER:	WN29922 Longitudinal Amyloid PET Substudy
VERSION NUMBER:	2
EUDRACT NUMBER:	2017-001364-38
IND NUMBER:	102,266
TEST PRODUCT:	Gantenerumab (RO4909832)
MEDICAL MONITOR:	*Ferenc Martenyi*, M.D.
SPONSOR:	F. Hoffmann-La Roche Ltd

I agree to conduct the study in accordance with the current protocol.

Principal Investigator's Name (print)

Principal Investigator's Signature

05/SEP/2018
Date

Please return the signed original of this form as instructed by your local study monitor. Please retain a signed copy for your study files.

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Regulatory Binder

- Documents Related to Study Participants
  - Informed Consent and Revisions
  - Informed Consent Logs
  - Signed Informed Consents
    - May be in the Participants Study File
  - Documentation of LAR/ Statement of Local Regulations
  - Participant Logs
    - Prescreening and Screening
  - Eligibility Review Worksheets
  - Source Document Forms
  - Approved Recruitment Materials

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INFORMED CONSENT TRACKING LOG

PROTOCOL TITLE:		
PROTOCOL NO.:	PRINCIPAL INVESTIGATOR:	SITE NAME:

Subject ID	Subject Initials	ICF version ref. (include language used)	Informed Consent Date	ICF version ref. (include language used)	Informed Consent Date	ICF version ref. (include language used)	Informed Consent Date

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13.3 Legally Authorized Representative (LAR)

A Legally Authorized Representative (LAR) is defined by 45 CFR 46.102(c) and 21 CFR 50.3 as *"an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research."*

Who may serve as LAR is determined by state law. Under Mississippi law, the order of authority to provide consent on behalf of another is as follows:

- Heath care agent
- Court-appointed guardian
- The spouse, unless legally separated
- An adult child
- A parent
- An adult brother or sister

A Legal Guardian is a person appointed by a court of appropriate jurisdiction.

When the UMMC IRB serves as the IRB of record for external sites and the use of LARs is proposed, information regarding relevant state law and local policy will be sought (local context information) and applied.

LARs should be well informed regarding their roles and responsibilities when asked to provide surrogate consent. In addition to the consent information, LARs should be informed that their obligation is to try to determine what the potential participant would do if able to provide consent, or if the potential participant's wishes cannot be determined, what they think is in the person's best interest.

Investigators must describe the intended use of LARs in their submission to the IRB. The IRB determines whether the use of LARs is appropriate for a given research study.
Further discussion and procedures for assessment of capacity and inclusion of adults with impaired decision-making capacity in research are described in Section 14.7.

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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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Subject Eligibility Checklist

Protocol Name/Number:		
Investigator Name:	Phone:	
Subject Name:	DOB:	Gender:
Eligible: Yes ☐ No ☐ (See Instructions Below) If not eligible, provide reason:		
Screened by: Signature: _____ Date: _____		

INCLUSION CRITERIA (To be eligible, all must be answered Yes)	Yes	No
1.	☐	☐
2.	☐	☐
3.	☐	☐
Etc.	☐	☐

EXCLUSION CRITERIA *(To be eligible, all must be answered No)*	Yes	No
1.	☐	☐
2.	☐	☐
3.	☐	☐
Etc.	☐	☐

Review by Investigator: Signature: _____ Date: _____

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Protocol: _____ Site No.: _____ Subject No.:_____ Visit: _____

Subject Visit Tracking Log

Subject ID	Consent Date	Baseline	Week 1	Week 2	Week 4	Final Status	Comments

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Source Documents

- “Source documentation is the beginning of a clean, verifiable audit trail.”

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Source Documents

- Source documents are used to:
  - Confirm the study participant exists
  - Confirm the reported study data is accurate (data integrity).
  - Confirm the study is conducted according to the protocol
  - Confirm compliance with Principles outlined

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What is source documentation

- ICH E6 1.52 source documents Original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, X-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).

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What is source documentation

- A source document is first instance a data point is recorded.

**Thus it is highly recommended that you create your own data collection tool.

Otherwise….

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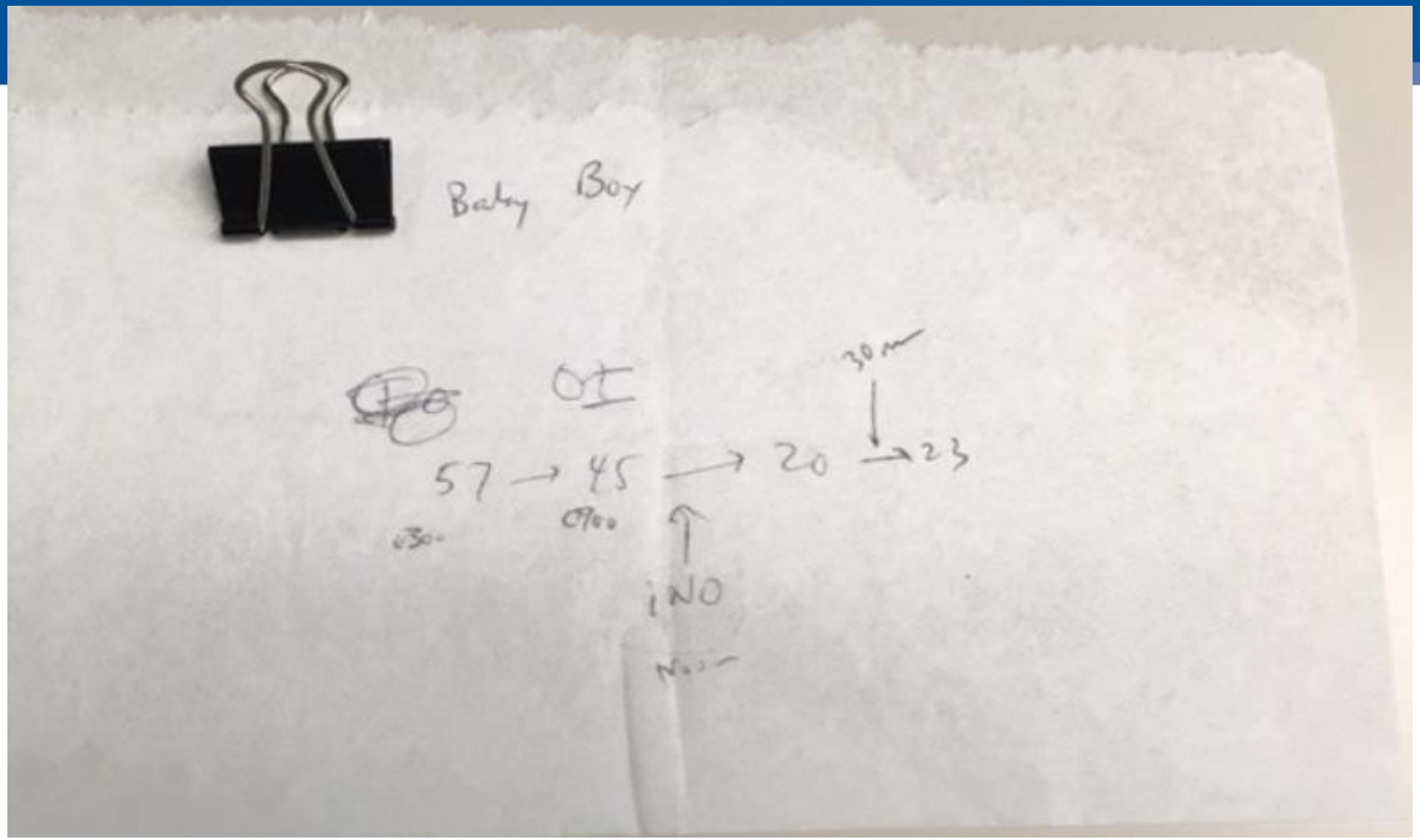

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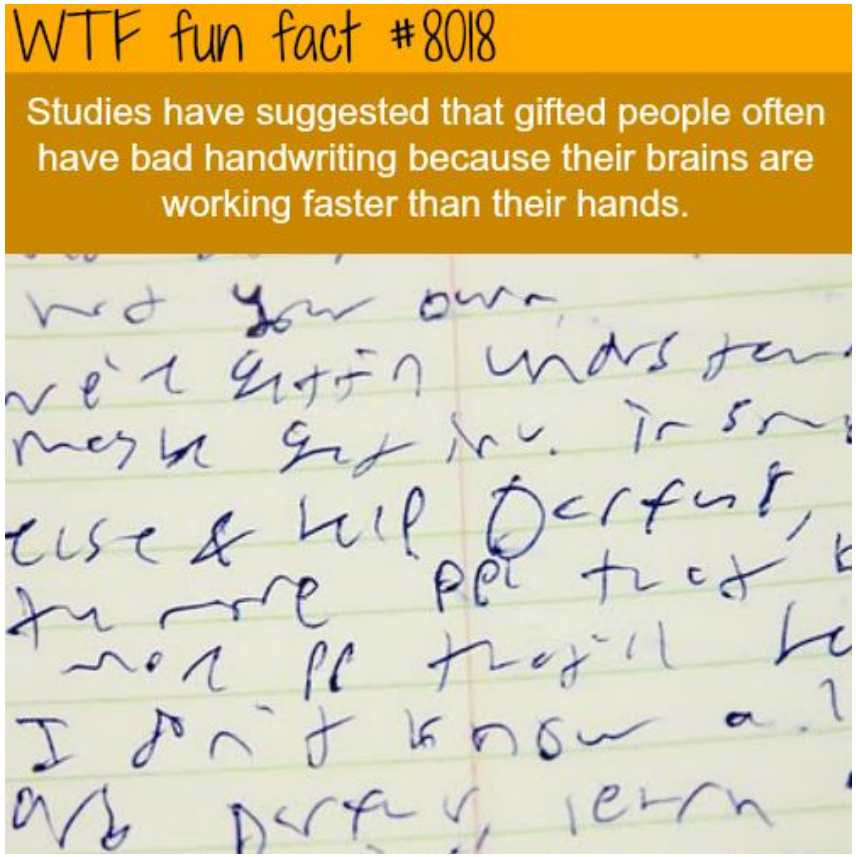
Good Source Documentation

- A - Attributable
- L - Legible
- C - Contemporaneous
- O - Original
- A - Accurate



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Preparing a source document plan

- Review your protocol for your key data points and work out where you will first record / obtain this data.
- The EDC is also helpful in creating source docs.

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Preparing a source document plan

Source data	Source documents – types
Blood pressure measurement	Medical record or participant study file or Direct onto case report form or Automated monitor printout
'Quality of Life' questionnaire responses	Participant diary (paper/electronic) or Direct onto case report form
Survey question response	Survey form completed by participant or interviewer
Record of study drug (tablet) taken at/between study visits by participant	Participant diary (hardcopy or electronic device), pharmacy dispensing log
Dose of study drug – calculation	Drug calculation worksheet, Medical Record

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Preparing a source document plan

- There should only be one source defined at any time for any data item.
- With regards to electronic source data, the earliest record that it is practical to retain should be considered as the location of the source data and therefore the source document.
- With regards to using an electronic medical record (EMR) for source data, it is preferable to list the actual location within the EMR for each parameter. This will increase efficiency of Monitors by reducing monitoring time and decreasing data queries.

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PATIENT STUDY ID #:_____ VISIT DATE:_____

BN29552 SCREENING VISIT

I. Investigator and Site Information
II. Subject Eligibility
III. RBR Research Sample Informed Consent
IV. IVRS
V. Visit Date
VI. Inclusion/ Exclusion Review
VII. FCSRT
VIII. MMSE
IX. CDR
X. ADAS-Cog 13
XI. Diagnostic Verification Form
XII. 12-Lead EKG
XIII. Physical and Neuro Exam
XIV. Vital Signs
XV. Lab sampling
XVI. Pregnancy Test
XVII. Amyloid Assessment Method
XVIII. Demographics
XIX. Caregiver
XX. Employment & Education
XXI. Tobacco use
XXII. Alcohol use
XXIII. Female Reproductivity
XXIV. Male Fertility
XXV. Surgeries and Procedures
XXVI. Medical History
XXVII. Concomitant Meds
XXVIII. Immunization Log
XXIX. Pneumonia Risk Factors

PATIENT STUDY ID #:_____ VISIT DATE:_____

Investigator and Site Information

Investigator Last Name: _____

Investigator First Name: _____

Investigator Number: _____

Site Number: _____

Date Investigator Assignment was Recorded: _____

Is this the Current Investigator? _____

Subject Eligibility

Date subject or legal guardian signed protocol informed consent

_____

Protocol Version: _____

RBR Research Sample Informed Consent

Did the subject consent to sample collection? Yes

No

Date subject/ legal guardian signed research sample informed consent:

_____

Consent type: _____

IVRS

Screening Number: _____

Screening Date: _____

Visit Date

Visit Date: _____ **Not Done (?):** _____ **Age:** _____

Protocol#: BN29553 SITE #: 300150

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FCSRT (Screening)

Was the FCSRT performed? Yes

No

Date Performed: _____

Score: _____

Completed By: _____

MMSE (Screening)

Was the MMSE performed? Yes

No

Date Performed: _____

Score: _____

Completed By: _____

CDR (Screening)

Was the CDR performed? Yes

No

Date Performed: _____

Score: _____

Completed By: _____

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PATIENT STUDY ID #:_____ VISIT DATE:_____

Vital Signs (Screening)

Were any vital signs collected at this visit? Yes

No

Vital signs date: _____

Temperature: _____ **Temperature Unit:** _____

Pulse: _____ **Pulse Unit:** _____

Respiratory Rate: _____ **Respiratory Rate Unit:** _____

Position of Blood Pressure measurement: Sitting

Supine

Semi-supine

Sit Time Start: _____ **Site Time End:** _____

Systolic Blood Pressure: _____ **Diastolic Blood Pressure:** _____

Weight: _____ **Weight Unit:** _____

Height: _____ **Height Unit:** _____

Oxygen Saturation: _____ **Oxygen Saturation Unit:** _____

***** SIT TIME MUST BE AT LEAST 15 MINUTES *****

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PATIENT STUDY ID #:_____ VISIT DATE:_____

12-Lead EKG

Was EKG (triplicate) performed? Yes

No

EKG 1 Date: _____

EKG 1 Time: _____

EKG 2 Date: _____

EKG 2 Time: _____

EKG 3 Date: _____

EKG 3 Time: _____

SUPINE TIME START: _____

SUPINE TIME END: _____

Patient Lying Supine: YES

No

***** PARTICIPANT MUST BE RESTING SUPINE FOR AT LEAST 5 MINUTES *****

PATIENT STUDY ID #:_____ VISIT DATE:_____

Physical Examination

PHYSICAL EXAM - To Be Completed by Study Physician

Height _____ Weight _____ Pulse _____ Blood Pressure _____

Body System	Normal	Abnormal Findings	Initials
Skin			
HEENT			
Cardiovascular			
Gastrointestinal			
Endocrine Metabolic			
Genitourinary			
Neurological			
Blood Lymphatic			
Musculoskeletal			

I certify that I have examined this research participant on this date and found them medically qualified to participate in the research study.

Physician's Signature: _____ Date: _____

Physician's Address: _____

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Central Lab

Was lab assessment performed: Yes

No

Accession Number: _____

Collection Date: _____

Was the sample Collected? (Check all that apply)

	Serum chemistry: AST, ALT, alkaline phosphatase, total protein, total bilirubin, serum albumin, CPK, sodium, potassium, calcium, BUN/UREA, and serum creatinine (and creatinine clearance calculated by the central laboratory)
	HbA1c, folic acid, and vitamin B12, T4, free T4, and thyroid-stimulating hormone levels will also be assessed as per the schedule of assessments
	Hematology: hemoglobin, hematocrit, RBC (with morphology), WBC counts, platelet, basophil, eosinophil, lymphocyte, monocyte, neutrophil, and WBC–other total counts
	Screening serologies: HIV, hepatitis B, hepatitis C
	Coagulation: PT
	Immunophenotyping: including CD4, CD8, CD3, CD19, CD16 +56
	Urine for drugs of abuse: At screening only, urine samples will be analyzed for the presence of the following drugs: amphetamine, benzodiazepines, cannabinoids, opiates, cocaine, barbiturates, and methadone.
	Urinalysis will be performed at the site by dipstick for blood, protein, glucose, and pH. Microscopic examination performed at the central laboratory if blood and/or protein results are positive or strongly positive. Results do not need to be recorded on the eCRF.
	Urine for pregnancy: Urine pregnancy testing will be performed at each dosing visit for women of childbearing potential (including those who have had a tubal ligation), and at the site for any other female participants if required by local regulations. If a urine pregnancy test is positive, it must be confirmed by a serum pregnancy test at the central laboratory.

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PATIENT STUDY ID #:_____ VISIT DATE:_____

Reproductive Status-Male

Is male fertile: YES

No

Unknown

If yes, does male agree to use contraception? Yes

No

N/A

If no, does male agree to remain abstinent (per protocol)? YES

No

N/A

Male Fertility Status:

_____

Agreement to use contraception:

_____

_____

_____

Agreement to remain abstinent;

_____

_____

_____

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Amyloid Assessment Method (Screening)

CSF: _____

PET: _____

Test not performed: _____

(Check all that apply)

Date: _____

Results in Source: Yes

No

MRI (Screening)

Was the MRI Performed? Yes

No

Date: _____

Results in Source: Yes

No

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Regulatory Binder

- Investigator's Brochure
  - Investigator's Brochures and Addendums
  - IB Acknowledgements and Receipts

IB

is a shorter form of

Investigator's Brochure

by allacronyms.com

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Regulatory Binder

- IRB
  - IRB Composition*
  - IRB Federal Assurance Number
  - Initial Submission and Approval
  - Notifications/ Submissions/ Approvals during the study
    - Continuing Reviews, Amendments, etc.
  - IRB closure documentation
  - Other specific IRB submission documentation
    - Radiation Safety Forms
    - Biosafety Committee Forms

IRB

Institutional Review Board

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Policy on IRB Rosters

The Institutional Review Boards (IRB) for the University of Mississippi Medical Center have an approved assurance with the Office for Human Research Protections (OHRP). Each IRB is registered with OHRP, and membership lists are filed, as required. Membership lists are not distributed or shared.

Each IRB abides by all applicable human research regulations including 45 CFR 46 and, where appropriate, 38 CFR 16, 21 CFR 50, 56 and ICH guidance as adopted by the FDA.

In accordance with these regulations no IRB member is allowed to participate in the discussion or vote of the IRB review of any study in which the member has an interest.

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Regulatory Binder

- Monitoring and Site Management
  - SIV Attendance Log & SIV Report
  - Site Visit Log
  - Site Visit Confirmation Letters
  - Site Visit Follow-Up Letters
  - Newsletters
  - Mass (Study Wide) Correspondence
  - Essential Site Correspondence (emails)
  - Protocol Deviation Logs

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Monitoring Visit Log

Investigator Name:	Protocol:	Site Number:

Name	Signature	Purpose of Visit	Date of Visit

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Protocol Deviation Tracking Log

Protocol ID/Number:		**Site Name/Number:**	
Protocol Title (Abbreviated):			
Principal Investigator:		**Page number [1]:**	

Ref No.	Subject ID	Date of Deviation	Date Identified	Deviation Description	Dev. Type [2]	Resulted in AE?	Did Subject Continue in Study?	Meets IRB Reporting Req. (Yes/No)	IRB Reporting Date
1									
2									
3									
4									
5									

Investigator Signature: _____ **Date:** _____

Version 2.0 – 2013-04-23

Check if final page of log: ☐

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Regulatory Binder

- FDA Documents
  - FDA 1572/1571 Forms
    - FDA Form 1572 for IND studies
    - FDA Form 1571 for investigator-initiated INDs
  - FDA Document History Log
    - Tracks all correspondence submitted to the FDA.
  - Financial Disclosure Forms (FDF's)
    - Signed financial disclosure forms (FDF) for the principal investigator and sub-investigator(s) listed on Form 1572

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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: August 31, 2011
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 Sponsor/Applicant/Submitter or Other

Address 1	Address 2	
City	State	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	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	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	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

8. PROVIDE THE FOLLOWING CLINICAL PROTOCOL INFORMATION. *(Select one or both 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.)

Public reporting burden for this collection of information is estimated to average 100 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of the Chief Information Officer
1350 Piccard Drive, Room 400
Rockville, MD 20850

Please DO NOT RETURN this application to this address.

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 control number.

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FDA Document History Log

Investigator Name:	Protocol:	IND Number:

List all documents submitted to the FDA.

Date of Correspondence	Type of Correspondence (i.e., submission, contact report, etc.)	Serial Number (If applicable)	Description

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: December 31, 2015

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if appropriate)) submitted in support of this application, I certify to one of the statements below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable check box.

☐ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator had a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
FIRM/ORGANIZATION	
SIGNATURE	DATE *(mm/dd/yyyy)*

This section applies only to the requirements of the Paperwork Reduction Act of 1995.

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 control number. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Do NOT send your completed form to the PRA Staff email address below.

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
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."

PSC Publishing Services (301) 443-6740 EF

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form Approved: OMB No. 0910-0396
Expiration Date: December 31, 2015

TO BE COMPLETED BY APPLICANT

The following information concerning _____ , who participated
Name of clinical investigator

as a clinical investigator in the submitted study _____
Name of

_____ is submitted in accordance with 21 CFR part 54. The
clinical study

named individual has participated in financial arrangements or holds financial interests that are required to be disclosed as follows:

Please mark the applicable check boxes.

☐ any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;

☐ any significant payments of other sorts made on or after February 2, 1999, from the sponsor of the covered study, such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;

☐ any proprietary interest in the product tested in the covered study held by the clinical investigator;

☐ any significant equity interest, as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

NAME	TITLE
FIRM/ORGANIZATION	
SIGNATURE	Date *(mm/dd/yyyy)*

This section applies only to the requirements of the Paperwork Reduction Act of 1995.

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 control number. Public reporting burden for this collection of information is estimated to average 5 hours per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Do NOT send your completed form to the PRA Staff email address below.

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
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."

PSC Publishing Services (301) 443-6740 EF

Regulatory Binder

- Investigator and Site Personnel
  - Confidentiality Agreement (CDA)
  - Delegation of Authority (DOA) Log
  - Signed CV's of Site Staff
    - Within the last 2 years*
  - GCP Certifications
  - Training Records and Logs
    - Training is done throughout the study
  - Qualification Documentation
    - MD, RN, RT, MA, etc. licenses
  - CTA

UMMC Research

Delegation of Authority Log

STUDY NAME

Site Number: ____

The purpose of this form is to: a.) serve as the Delegation of Authority Log and b.) ensure that the individuals performing study related tasks/procedures are appropriately trained and authorized by the Investigator to perform the tasks/procedures. This form should be completed prior to the initiation of any study-related tasks/procedures. The original form should be maintained at your site in the study regulatory/study binder. This form should be updated during the course of the study as needed.

Please Print	Obtain Informed Consent	Source Document Completion	Case Report Form (CRF) Completion	Assess Inclusion and Exclusion Criteria	Physical Examination	Medical History	Medication History / Concomitant Medication	Collect Vital Signs	Review Vital Signs and Labs for Clinical Significance	Laboratory Specimen Collection/Shipping	AE Inquiry and Reporting	AE/SAE interpretation (severity/relationship to IP)	Administration of Investigational Product (IP)	IP Accountability	Regulatory Document Maintenance	Administrative	
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:

I certify that the above individuals are appropriately trained, have read the Protocol and pertinent sections of 21CFR 50 and 56 and ICH GCPs, and are authorized to perform the above study-related tasks/procedures. Although I have delegated significant trial-related duties, as the principal investigator, I still maintain full responsibility for this trial.

Investigator Signature: ____ **Date:** ____

Site Signature Log/Delegation of Authority Log Version 2.0

SO WHO NEEDS TO BE ON THE DOA?

- The bedside nurse drawing standard of care labs for a participant enrolled in a study?
- The person transferring de-identified echocardiograms for a clinical trial to the study Sponsor?
- An MRI tech doing a brain scan following a research protocol?
- An RT setting up CPAP for a patient with OSA who is enrolled in a stroke study?

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Training Log

Investigator Name:	Protocol:	Site Number:

Printed Name	Signature	Title of Training	Date of Training

UMMC Research

Regulatory Binder

- Study Medication*
  - Pharmacy Manual
  - Shipping Records
  - Drug Accountability Log
  - IP Temperature Log
  - Study Medication Return/ Destruction
  - IVRX User Guidelines
  - IP Labels

UMMC Research

Investigational Product Accountability Log: Stock Record

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

Line No.	Date	Dispensed To / Received From	Dose	Quantity Dispensed and/or Received	Balance Forward / Balance	Lot No.	Recorder's Initials
Ex.	*15Feb2012*	*Manufacturer*	*10 mg*	*+ 100 tabs*	*500 / 600*	*98765*	*JAD*
1.							
2.							
3.							
4.							
5.							
6.							
7.							
8.							

UMMC Research

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.								

UMMC Research

Regulatory Binder

- Laboratory Manual
- Acknowledgement of receipt forms
- Temperature Logs
- Bio sample Inventory Logs
- Correspondence with Central Laboratory
- CLIA Certification and CAP accreditation
  - Ensures your test results are meeting and exceeding industry standards for clinical laboratory testing
- Lab reference ranges*
- Specimen Tracking Logs


Updated Lab ranges.pdf


Batson Lab Ranges.pdf

UMMC Research

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

UMMC Research

Regulatory Binder

- Serious Adverse Events Reporting and Safety
  - SAE Forms and Reporting Instructions
  - SAE related correspondence
    - IRB and Sponsor
  - Safety Reports
    - Including SUSAR's
  - Confirmation of notification of safety related issues
    - Signed by the PI

UMMC Research

National Center for Complementary and Integrative Health

Serious Adverse Event (SAE) Report Form

STUDY NAME

Protocol Number:_____

Site Name:_____

Pt ID:_____

Date Participant Reported:

__ __ / __ __ __ / __ __ __ __
d d m m m y y y y

1. SAE onset date: __ __ / __ __ __ / __ __ __ __ (d d m m m y y y y)
2. SAE stop date: __ __ / __ __ __ / __ __ __ __ (d d m m m y y y y)
3. Location of SAE:_____
4. Was this an unexpected adverse event? ☐Yes ☐No
5. Brief description of participants with no personal identifiers:
   Sex: ☐F ☐M Age: _____
   Diagnosis for study participation:_____
6. Brief description of the nature of the SAE (attach description if more space is needed):
7. Category of the SAE:
   - ☐ Date of death ___/____/_____ (dd/mmm/yyyy)
   - ☐ Life threatening
   - ☐ Hospitalization – initial or prolonged
   - ☐ Disability/incapacity
   - ☐ Congenital anomaly/birth defect
   - ☐ Required intervention to prevent permanent impairment
   - ☐ Other:_____
8. Intervention type:
   - ☐ Medication or nutritional supplement (specify):_____
   - ☐ Device (specify):_____
   - ☐ Surgery (specify):_____
   - ☐ Behavioral/lifestyle (specify):_____

9. Relationship of event to intervention:
   - ☐ Unrelated (clearly not related to the intervention)
   - ☐ Possible (may be related to intervention)
   - ☐ Definite (clearly related to intervention)
10. Was study intervention discontinued due to event? ☐Yes ☐No
11. What medications or other steps were taken to treat the SAE?
    _____
12. List any relevant tests, laboratory data, and history, including preexisting medical conditions:
    _____
13. Type of report:
    - ☐ Initial
    - ☐ Follow-up
    - ☐ Final

Signature of principal investigator: _____ Date: _____

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Adverse Event Log

Protocol: (Insert title or protocol number here)

Subject ID:_____

Adverse Event:	**Adverse Event:**
Serious Criteria Met? Yes: ☐ No:☐	**Serious Criteria Met?** Yes: ☐ No:☐
Onset Date:	**Onset Date:**
Onset Time (24hr clock):	**Onset Time** (24hr clock):
Severity: ☐Mild ☐ Moderate ☐ Severe	**Severity:** ☐Mild ☐ Moderate ☐ Severe
IP Dose Action Taken: ☐None ☐ Stopped Temporarily ☐Increased ☐Permanently discontinued ☐Reduced **Concomitant Medication Action Taken:** ☐None ☐ Stopped Temporarily ☐Increased ☐Permanently discontinued ☐Reduced	**IP Dose Action Taken:** ☐None ☐ Stopped Temporarily ☐Increased ☐Permanently discontinued ☐Reduced **Concomitant Medication Action Taken:** ☐None ☐ Stopped Temporarily ☐Increased ☐Permanently discontinued ☐Reduced
Subject Action Taken: ☐Withdrawn ☐Other, Specify: _____ ☐Treatment Given ☐None	**Subject Action Taken:** ☐Withdrawn ☐Other, Specify: _____ ☐Treatment Given ☐None
Causality: Related to study treatment : ☐Yes/Unknown ☐No If No, what was the most likely cause: ☐Disease under study ☐Background study drug: Specify _____ ☐Concomitant treatment: Specify _____ ☐Other: Specify _____ ☐Injection/procedure related:☐ **Investigator Signature & Date:**_____	**Causality:** Related to study treatment : ☐Yes/Unknown ☐No If No, what was the most likely cause: ☐Disease under study ☐Background study drug: Specify _____ ☐Concomitant treatment: Specify _____ ☐Other: Specify _____ ☐Injection/procedure related:☐ **Investigator Signature & Date:**_____
Is the AE ongoing at the end of the study? ☐Yes ☐No **If No, Stop date:**	**Is the AE ongoing at the end of the study?** ☐Yes ☐No **If No, Stop date:**
Comments:	**Comments:**

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16.2 Procedures

16.2.1 Reporting

Adverse events in clinical trials must be reported to the sponsor in compliance with FDA regulations and sponsor requirements. Unless specifically required by the IRB for a given protocol, the UMMC IRB does not accept reports of adverse events that are not UPs.

With one exception, noted below, Investigators must report the following events or issues to the IRB as soon as possible but within 10 business days after the investigator first learns of the event using the Unanticipated Problem form in the IRB electronic system. Note: The study-related death of a UMMC research participant must be reported within 48 hours of notice. If investigators are uncertain but believe that the event might represent an UP, a report should be submitted.

UMMC Research

Regulatory Binder

- Data Management
  - eCRF Guidelines
  - eCRF Pages (Unique Forms)

UMMC Research

Regulatory Binder

- Equipment and Study Materials
  - Equipment Calibration Log
  - Equipment Certificates
  - Study material and Equipment receipt forms

UMMC Research

	TITLE:	MEASUREMENT AND TEST EQUIPMENT CONTROL AND CALIBRATION IDENTIFICATION ATTACHMENT 1
Department:		DATE

EQUIPMENT CALIBRATION INFORMATION

Description	Manufacturer	Model & Serial No. or Unique Id No.	Calibration Required	Calibration Frequency	Comments

UMMC Research

Regulatory Binder

- Correspondence
  - Study and Vendor Team Contact Information
- Other
  - Note to Files
  - General Memo's

UMMC Research

Regulatory Binder

- Note to File
  - Why do we write NTF's
    - Identify a discrepancy or problem in the conduct of the clinical research study
    - Note the root cause of the identified problem
    - Identify a corrective action taken to prevent recurrence of a problem
    - Document that the corrective action has resolved the problem
  - Note to Study File may be appropriate to:
    - Clarify or add information regarding site-specific regulatory file requirements
    - Clarify or add information regarding source document standards
    - Document and address any issue that is protocol/ site-specific that cannot be resolved without a change from previous procedures.

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Sample Note To File:

PROTOCOL #: 2010-01000

TITLE: The Effect of 'Investigational Product' on XYZ Levels in Healthy Controls

From: research coordinator
[Insert staff name, include role on study}

To: Subject File

Re: Subject# 015-SAW
[insert subject identification]

Date: October 31, 2011

Dr. Smith consented the subject on January 20, 2010. Dr. Smith, in error dated the consent form January 22, 2010. The dating discrepancy is not representative of an inappropriate consent process, but the result of a typo. Dr. Wolf has been reminded to confirm the correct date in the future.

Signature:

UMMC Research

Data Correction

- Case Study
  - Your monitor notes that your principal investigator documented examining a study subject on April 7th, 2014. You completed the paper-based case report form (CRF) for the corresponding visit and indicated that the visit took place on May 6th, 2014 (4/7/14 vs. 5/6/14). After review, you confirm that the visit took actually occurred on May 7th, 2014 and need to correct your CRF.

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Data Correction

- Do You?
  - A. Scribble out the date you wrote and then write the correct one next to it
  - B. Try to change the date that you wrote by writing over the numbers to indicate 4/7/14
  - C. Draw a line through the previously written date, initial and date next to it, then write the correct date of 4/7/14
  - D. Use correction tape to go over the previous date and then write the correct date over it
  - E. Leave it alone, the monitor doesn't know what they are talking about

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Data Correction

- Why is this the correct way?
  - "Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained)." -International Conference on Harmonization Good Clinical Practice (ICH GCP E6 Part 4.9.3)

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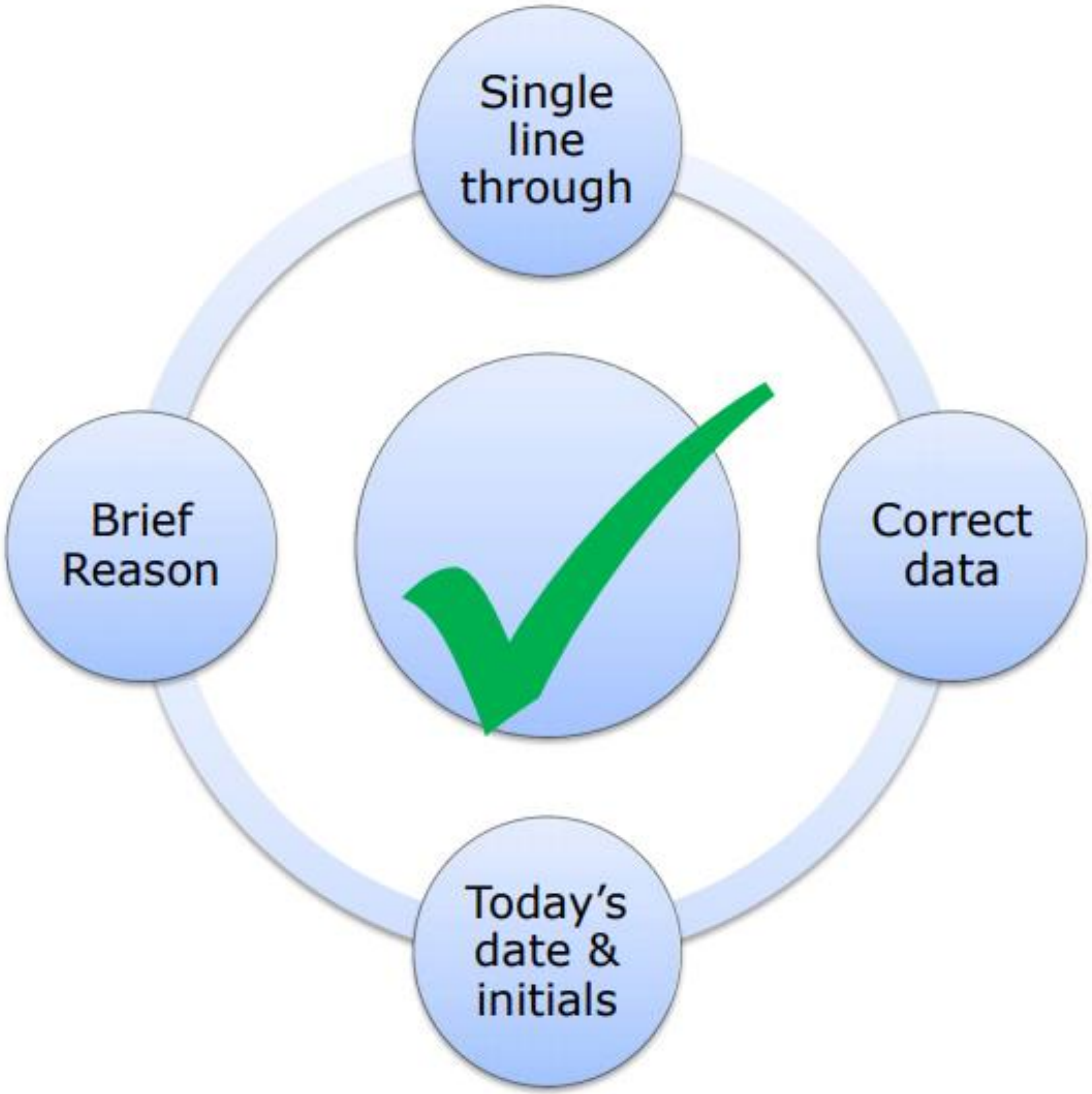
Corrections

UMMC Research

Corrections



UMMC Research

References and Tools

- https://nccih.nih.gov/grants/toolbox
  - Forms
    - Data and Safety Management
    - Study Accrual and Retention Plan
    - Protocol Template
    - Case Report Forms
    - Protocol Associated Documents
    - Essential Documents/ Regulatory Binder
    - Pharmacy and Investigational Product

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