Source Documentation Standards for DMID Clinical Studies
Source Data Defined

• “All information in original records and certified copies of original records…. necessary for the reconstruction and evaluation of the trial.”

» ICH GCP 1.51
Source Documents May Include:

- Hospital records, Clinic charts
- Laboratory notes
- Memoranda
- Subject diaries
- X-rays
- Subject files

» ICH GCP 1.52
Documentation of Source Data

• Necessary for reconstruction, evaluation and validation of clinical findings
• Substantiates integrity of trial data
• Confirms observations, existence of subjects
• Ensures data quality by creating an audit trail
Documentation of Source Data

• Data recorded on Case Report Forms (CRFs) should be consistent with the Source Documents (Any discrepancies should be explained)
• For more information visit
  – www.ich.org
  – www.fda.gov
Source Document Standards

• Aid in establishing a system of records
• Based on ICH/GCP, CFR, and guidances that apply to the involvement of Human Subjects
• Applicable to all DMID funded clinical trial sites
Document Layout

- Table of Contents
  - Alphabetic by topic
  - Methods/Procedures
  - Adequacy criteria
  - Requirements
  - DMID allowable methods
  - Recommendations

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Exception to the Standards

• Sites participating in multi-center or industry sponsored IND trials
  – Consult MOP and source document workbooks
  – Study-specific source documentation workbooks may be provided

• Local, state, institution, institutional review board (IRB), standards may differ
  – Always follow the more stringent standard
Correcting Records

• One line through, write new data, initial, date, and explain (if necessary)
• Changes made by original entry person or other authorized person
• Unacceptable correction methods
  – obliterations, correction fluid
Addenda to Source Documentation

• When Source Documentation is found to be incomplete (by site staff, monitor, auditor), document the deficiency in a chart note

• Addenda must be dated and initialed in “real time” in the Source Document

• Addenda must be made by research clinician presently responsible for the subject
Awareness Check

• How would you add documentation of a missed visit in source documents?
  – Example
CRF

- Tool to collect the data and provide a condensed picture of the participant’s involvement in the study
When used as a Source Document

• Must be identified in the Protocol, MOP, or SD agreement before the study begins
• Use original, signed, credentialed and dated CRF
• Site designed study forms must allow for free form text entry
Awareness Check

• You are using a CRF as the source, but it is not identified in the Protocol or MOP.
  – What do you do?
Communication

• Verbal
  – Telephone verification of subject diagnoses or events with outside clinicians should be documented in a contact report

• Written
  – Correspondence must include appropriate study subject identifier's so monitor can verify that documents correspond to particular study subjects
Confidentiality

- Informed consent process assures:
  - Records will remain confidential to the extent permitted by law
  - Records will be identified by code (PID)
  - Study information will not be released without subjects written permission
  - Subject will not be personally identified in any publication about the study
Contraception Documentation

• Protocol-specific and/or IRB-required counseling must be documented
• Current form of contraception must be documented
• Informed Consent Form must be signed acknowledging any contraception requirements.
Certified Copies

- A copy of original information that has been verified, by dated signature or initials and certification statement, that the document is an exact copy having all of the same attributes and information as the original.
Certified Copies

• If an original document is retained on-site or within an institution, a copy needs to be certified
• There should be an identifier on the document indicating where the document originated
• Documentation received via FAX is not considered original, and must be certified
• Activity
What do you do if the sending institution does not certify the copy?

• Receiving institution verifies the copy is “unaltered as received”

• Verifier must sign, or initial and date a statement on the copy indicating it is “unaltered as received”

• Statement may be in the form of a stamp, as long as it is accompanied by an original signature or initials and date
• The site has received a discharge summary via fax from a health care facility where a study subject was treated over the weekend for angina. The fax is difficult to read and looks as if some information has been covered with correction fluid (white-out).
  – Should the coordinator certify this copy?
  – What does the certification mean?
Death Documentation

• Verify date and cause of death with:
  – Autopsy report
  – Obituary
  – Death Certificate

• If official documents are not available:
  – Document verbal communication with a physician, study subject family member or friend to verify date and cause of death
What is a Protocol Deviation

• Any noncompliance to the Protocol, Good Clinical Practice (GCP), or protocol-specific Manual of Procedures
  – Noncompliance may be either on the part of the subject, investigator, or study site staff.

• May result in significant added risk to the study subjects

• Interferes with the integrity of the data
Protocol Deviations

- Occur when there is non-adherence to the Protocol, including Informed Consent and Enrollment non-adherence. Other deviations could be:
  - Missed visits
  - Failure to obtain scheduled lab draw
  - Administration of non-permitted concomitant medications

* DMID does not allow any exemptions or eligibility criteria wavers for enrollment.
Documenting Deviations

• Address in study subject Source Documentation
• Include reasons and prevention attempts
DMID Reporting Requirements

• Must be reported within 5 working days of identification of the protocol deviation, or within 5 working days of the scheduled protocol-required activity.
3 Ways to Report Protocol Deviations

1. Protocol Deviation Web Form
2. Protocol Deviation Print Form and Fax Cover Sheet
3. Email the Protocol Deviation Print Form and Fax Cover sheet
1. Protocol Deviation Web Form

- Complete the web-based Protocol Deviation form on the web and submit via the DMID-CTM website, https://www.dmidctm.com/partners/

<table>
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<th>Protocol Deviation Web Based Form</th>
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<tr>
<td>Deviation Date: (dd/mm/yyyy)</td>
</tr>
<tr>
<td>Person Submitting Form:</td>
</tr>
<tr>
<td>Email Address:</td>
</tr>
<tr>
<td>Site Name:</td>
</tr>
<tr>
<td>Investigator Name:</td>
</tr>
<tr>
<td>DMID Protocol Number:</td>
</tr>
<tr>
<td>Alternate Protocol Number (if applicable):</td>
</tr>
<tr>
<td>DMID Protocol Title or Short Name:</td>
</tr>
<tr>
<td>If the deviation is not associated with a particular subject, Please click here:</td>
</tr>
<tr>
<td>N/A (and skip to 'Brief Deviation Description' below)</td>
</tr>
<tr>
<td>If the deviation is associated with a particular subject, complete the following:</td>
</tr>
<tr>
<td>Subject Number(s):</td>
</tr>
<tr>
<td>Complete the following three questions only if the Deviation was associated with a Subject Number(s).</td>
</tr>
<tr>
<td>Did the Deviation result in an adverse event?</td>
</tr>
<tr>
<td>Did the Deviation result in a serious adverse event?</td>
</tr>
</tbody>
</table>
2. Fax Protocol Deviation Form

1. Print the Protocol Deviation Form
2. Complete the form
3. FAX with the FAX transmittal form to: 1-888-311-3449; International Access Code is 13449.
3. Email Protocol Deviation Form

- SAVE the Protocol Deviation form and the email/FAX transmittal form to your computer or network
- Complete both forms electronically and email as attachments to: govngodmidprotocol.deviations@wilm.ppd.com
Reporting Deviations

• Sites must complete a copy of the DMID Protocol Deviation Form for each Protocol Deviation

• DMID Protocol Deviation Forms must be maintained in the Regulatory File as well as in the subject’s Source Documentation

• Copies of fax confirmation or e-mail printout that Protocol Deviation Forms were submitted need to be included.
Central Unit or Coordinating Center

• Deviations will be reported as specified in the respective Protocol or MOP.
  – The Central Unit will report the deviation information to PPD
Protocol Deviation Report Flow

EMMES-IDES (If applicable) → Site → PPD-CTM → DMID → Central Unit (if applicable) → IRB (required)

Distributed to:
- Protocol Champion
- Program Officer
- Regulatory Affairs Specialist
- Medical Monitor
- Clinical Monitoring Coordinator
Awareness Check

• How do you handle protocol deviations at your location?

• What are some of the most common protocol deviations?
Electronic Medical Records

- Sites may either printout a copy of the medical records or provide access to an institutional computer for the monitor’s review

- Printout must include institutional name and date
Multi Page Printouts

• The package of printouts is to remain intact in the file

• Each page must be initialed and dated to verify that it is part of a package

• First page must have:
  – Identifying information
  – Site staff initials
  – Date
  – Number of pages included in the printout
End Point Criteria

• For study defined endpoints:
  – Subject’s SD must document the specifics of the event and tests required by the protocol

• Lab or diagnostic reports
  – Must have an official header or letterhead identifying where the test was performed
End Point Documentation

• Print screen copy of electronic lab report with appropriate study subject identifiers, date of specimen collection, lab name, and date of printout

• Hard copy lab report from research/commercial lab with appropriate study subject identifiers and date of specimen collection

• Hard copy of correspondence that study subject has reached a study-defined lab-based end point
Documenting Labs

- Lab Printouts must include:
  - Institution lab name
  - Subjects name or study PID
  - Date of test
  - Date of printout
Entry Criteria Documentation

• Address each specific entry criteria
• Must be signed, credentialed, and dated by the enrolling clinician
Informed Consent

• Informed Consent must be signed and dated in ink by subject, parent/guardian/legally authorized representative prior to protocol screening

• Must correspond to the Protocol version approved by the IRB that was current at the time
Illiterate Parent/Guardian/Legally authorized representatives:

- Must have impartial witness during entire informed consent discussion
- All documents and written information must be read aloud and explained
- Allow opportunity for questions
- Must sign and personally date the consent form
Questionnaires

• Document indicating the study subject completed the form per Protocol Evaluation Schedule by:
  – Entering a note in the subject’s chart or CRF used as SD indicating the form used on a specified date
  – Indicating on a checklist the subject-completed form on a specific date
  – Including in the SD a copy of the subject-completed form that is signed and dated by the study personnel
Research Records

• All documents corresponding to a given study subject's participation in a clinical investigation including:
  – Signed Informed Consent
  – Source Documentation
  – Study prescriptions
  – Investigational Pharmacy Records
  – Case Report Forms (CRF)
Shadow Files

• Are certified copies of the subjects original lab reports, medical record, or clinical chart

• Are intended to reflect a complete study-specific record

• Monitors and auditors may request the original documents to verify validity of data or to look for unreported Adverse Events (AEs)
Medical Records that May be Included in a Shadow File

- Documentation of consent process
- Screening results
- Medical history/physical exam
- Vital status
- Clinical and lab findings
- Management of study drugs/agents and toxicities
- Concomitant medication
What are Toxicities?

- Toxicities are Adverse Events, Signs & Symptoms, or Abnormal Lab Results
Toxicities

• Must be documented in the CRF or in additional Source Documents

• For abnormal lab values, **clinical significance** must be documented by a responsible research clinician

• Research clinicians must note in the CRF/SD the relationship of the event to the Investigational Product unless otherwise specified in the Protocol
Awareness Check

• What possible actions should site personnel take upon the discovery of laboratory toxicity?
Urine Pregnancy Testing

• If your clinic/lab performs “waived” testing, but does not fall under a CLIA Certification of Compliance from a laboratory conducting moderate to high level testing, a CLIA Certificate of Waiver must be obtained
  - Examples: Urine pregnancy tests; urinalysis
Urine Pregnancy Test

• Document
  - When the test was done
  - Test results
  - Who performed or interpreted the results
Conclusion

• DMID applauds your COMPLIANCE to all Source Documentation Standards
• Questions can be directed to DMID or monitors during visits