RESEARCH 102
Session 4:

Creating Site Worksheets/ Visit Checklists

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Source Documents

- 1st place information is documented is the source
- Original documents, data and records, or original certified copies of original records of clinical findings and observations

Regulations/Guidance

21 CFR 312.62: Case Histories: an investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data including signed and dated consent forms and medical records (including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes). The case history for each individual shall document that informed consent was obtained prior to participation in the study.

ICH GCP E6, section 1.51 defines source data as "all information in original records and certified copies of original records or clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies.)."

ICH GCP E6, section 1.52 defines source document as "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 form automated instruments, copies or transcriptions certified after verification as being accurate and complete, 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 trials.)."

The data trail MUST lead back to the original source. No piece of data may be included in the body of research that cannot be found elsewhere.

Purpose of Study Documentation

- Document the rights, safety, and well-being of the subject was protected
- Ensure integrity of the data
- Show compliance with the protocol, regulations, guidance, policies and procedures

- Reconstruct the events of the trial
- Tell the story of the subject's participation
- Reconfirm data
- Provide an audit trail
- Subject's record of study participation
- Confirms eligibility
- Documents progress throughout the study
- Records events (IP accountability, consenting)

Examples of Source Documents

- Medical records
- Lab results
- Test results (x-ray, CT)
- Subject diaries, questionnaires
- Informed consent process documentation
- Vital signs// study procedures
- Physical exam
- *Research Notes / SSD / visit worksheets*

Source Documentation vs. SSDs

Not all source docs are research visit notes

But ALL research visit notes that you create are source documents!!

SITE source documents reflect research activity at your SITE

- Research visit procedure documentation/worksheets/checklists/logs
- ICP documentation
- Subject instruction sheets
- Progress notes
- Eligibility criteria worksheet / inclusion & exclusion checklist
- Concomitant medication log
- Adverse event log
- Communication log

How do I know what to include?

- Know the protocol, study the Schedule of Events table
  Request worksheets, CRFs/e-CRF screenshots as soon as possible
- Determine what can be found in other source documents
- What data points can ONLY be created by the interaction with the subject?

*Early in the study set up process, use worksheets and CRFs to guide you:

- understand what data to collect
- realize what data may be hard to find
- make a plan for how to capture it all

Components for SSDs

Header of the document:

- Study information, as applicable for your particular study
  - Protocol name, descriptor or identifying number
  - IRB#
  - PI
  - Sponsor
- Subject's study identifier (i.e. initials, study ID#)
- Visit type
  - Type of visit
  - Visit #

Department / Institution Logo or Name

Study: Wonder-Drug-Randomized Double Dlind . . . .
PI: John Doe
IRB#: 19-121345-FB,

Visit 1 / Screening
Subject Initials: _____
Subject ID: _____

Components (cont'd.)

Department Logo or Name

Adverse Event / Concomitant Medication Log

STUDY: Wonder Drug-Randomized, Double-Blind . . . .
PI: John Doe, MD
IRB#: 19-12345-FB

Subject Intitials: _____
Subject ID#: _____

Page_____ of _____

Components (cont'd.)

Body of the document,in checklist format:

- Date and demographics
- Eligibility met
- Informed Consent Process
- Study Procedures, in sequential order to be performed
- Closing note / education / next visit
- Progress note option
- Documentation of research staff and date of completion

Study Procedures

- VS completed by research staff
- Details about specimen collections
- Randomized, IP administration or dispensation, stickers
- IP return / compliance documentation
- Teaching / education
- Research specific procedures or testing (MoCA, 6" walk test, etc.)
- Specific procedures information to show protocol compliance
- Additional information for procedures not documented elsewhere

Other Forms to Create

- Inclusion / Exclusion checklist
- Informed Consent Process documentation / checklist
- Specimen logs
- Concomitant Medications / flowsheet
- Adverse Event flowsheet
- Communication log (interaction, communication, phone calls with participant)
- Blank progress notes

Protocol Eligibility

Inclusion criteria:

1. Provision of informed consent prior to any specific study procedures
2. Men or women $\geq$ 45 years of age
3. Acute ischemic stroke with randomization occurring within 24 hours after onset of symptoms.
   - National Institute of Stroke Score $\leq$ 10
4. Head Computed Tomography (CT) or MRI ruling out hemorrhage or other pathology.

Exclusion criteria:

1. Planned use of antithrombotic therapy including antiplatelets or herapin
2. Known hypersensitivity to wonder-drug or ASA
3. Any history of atrial fibrillation
4. Receipt of any thrombolysis (such as tPA) within 24 hours prior to randomization
5. Known severe liver disease
6. Pregnancy

Example: Protocol Eligibility

Inclusion / Exclusion

STUDY NAME
PI: John Doe, MD
IRB Number:

Subject Number:_____
Subject Initials:_____

INCLUSION (All Answers Must Be **Yes** To Enroll)

Yes	No	
☐	☐	1. Provision of informed consent prior to any study specific procedures
☐	☐	2. Male or female ≥ 45 years of age
☐	☐	3. Either acute ischemic stroke or high-risk TIA and randomization occurring within 24 hours after onset of symptoms
☐	☐	4. Head Computed Tomography (CT) or MRI ruling out hemorrhage or other pathology

EXCLUSION (All Answers Must Be **No** To Enroll)

Yes	No	
☐	☐	1. Planned use of antithrombotic therapy in addition to study medication
☐	☐	2. Known hypersensitivity to wonder drug or ASA
☐	☐	3. Any history of atrial fibrillation
☐	☐	4. Receipt of any thrombolysis within 24 hours prior to randomization
☐	☐	5. Known severe liver disease
☐	☐	6. Pregnancy

Enrolling Investigator Date

Example: Protocol Eligibility

Subject Eligibility Criteria Checklist

All subjects enrolled must meet eligibility criteria based on the inclusion/exclusion criteria detailed in the application and approved by the IRB.

I. Study Information

Protocol Title:	
IRB #:	
Principal Investigator:	
Sponsor:	

II. Subject Information:

Subject Initials/ID:
Gender: ☐ Male ☐ Female

III. Inclusion/Exclusion Criteria

Inclusion Criteria (From IRB-approved protocol)	**Yes**	**No**	**Supporting Documentation***
1.	☐	☐	
2.	☐	☐	
3.	☐	☐	
4.	☐	☐	
Exclusion Criteria (From IRB-approved protocol)			
1.	☐	☐	
2.	☐	☐	

*All subject files must include supporting documentation to confirm subject eligibility. The method of confirmation can include, but is not limited to, laboratory test results, radiology test results, subject self-report, and medical record review.

IV. Statement of Eligibility

This subject is **[☐ eligible / ☐ ineligible]** for participation in the study.

Signature:	Date:
Printed Name:	

Rechecking Protocol Eligibility

Inclusion criteria:

1. Provision of *informed consent **prior** to any specific study procedures*
2. Men or women $\geq$ *45 years of age*
3. Acute ischemic stroke with *randomization occurring within 24 hours after onset of symptoms.*
   - National Institute of Stroke Score $\leq$ 10
4. Head *CT or MRI* ruling out hemorrhage or other pathology.

Exclusion criteria:

1. Planned use of antithrombotic therapy including *antiplatelets or herapin*
2. Known *hypersensitivity to wonder-drug or ASA*
3. Any history of *atrial fibrillation*
4. Receipt of any *thrombolysis (such as tPA) within 24 hours* prior to randomization
5. Known severe *liver disease*
6. *Pregnancy*

ENROLLMENT VISIT

Visit 1_____

Subject ID#:_____

Subject Initials:_____

NAME OF STUDY

"A Randomized, Double-Blind Study with WonderDrug Compared to Aspirin (ASA) in Patients with Acute Ischemic Stroke"

IRB#:_____

PI: John Doe, M.D.

Screening Date: _____

Symptom Event Date_____ Onset Time_____:_____Duration:_____(hrs and min)

Date of birth: _____ Gender:_____ Race:_____

□ Hispanic or Latino □ Not Hispanic or Latino

□ Inclusion / Exclusion criteria reviewed per _____, MD, and deemed eligible to participate at this time.

□ Informed Consent process completed using ICF version _____. See ICP documentation checklist attached.

Subject desires to participate in genetic sub-study: □ Yes □ No

Informed Consent Form (version _____) given to subject / LAR. Subject/LAR was given ample time to read the Informed Consent Form. ICF explained and all questions answered to subject's/LAR's satisfaction. Voices understanding of intended purpose, subject requirements, possible risks, and benefits. Subject/LAR received a copy of the signed Informed Consent Form. Informed Consent Form completed per ICH GCP guidelines by: _____
Date:_____Time:_____:_____.

□ History and Physical completed per _____, MD (see medical records attached)

Weight _____lb kg Height:_____ cm in BMI:_____

□ Pulse: _____ Blood Pressure _____ / _____ mm/Hg

□ NIHSS per _____, MD (see attached)

□ EQ-5D questionnaire completed per_____(see attached)

□ Employment status of subject and caregiver completed per_____.

□ Concomitant medications documented (*See Concomitant Medication Flowsheet and MAR attached.*) Subject instructed to discontinue any medications listed as "restricted" per protocol as of today. Those medications include:

_____

□ Allergies:_____ □ NKA

□ CT or MRI performed: Date_____Time _____:_____

□ Current lab values attached □ ECG attached

□ Serum Urine pregnancy test completed for women of childbearing potential: Result_____ ☐ NA

IVRS contacted to confirm enrollment, obtain randomization number and kit number for study drug administration during this visit.

Kit Number: _____ **Batch No.:** _____ **Expiration Date:** _____

Date: _____**Time:** _____ **RZ Code:** _____

IP dispensed per protocol. Subject given detailed instruction and educational materials regarding medication and dosing schedule. Trial Information Card given to subject. Verbalizes understanding of all instructions. Encouraged to call with questions or concerns. Return appointment made for _____at ___:___. Detailed instructions for return visit given to subject. Subject reminded not to take medication on the morning of next visit for PK level - verbalizes understanding. Will call subject prior to next visit for reminder of appointment and instructions.

Additional Comments:

_____

_____

_____

Form Completed by:_____

Signature Date

ICP Initial Documentation

Screening Visit		
I. INFORMED CONSENT PROCESS (ICP)		
• The following persons were present for the IC process:		
• The consent form and study were explained by:		
• The cognitive ability of the subject was assessed by _____ and determined to the best of their ability to be capable • of making decisions for him/herself.	☐ YES	☐ NO
• All pertinent aspects of the study were explained including all of the information contained in applicable subparagraphs of section 4.8.10 of the ICG GCP E6 Guidance.	☐ YES	☐ NO
• The PI was available to answer questions, if needed.	☐ YES	☐ NO
• Did the subject request to speak to PI for additional information?	☐ YES	☐ NO
• The IC process was performed in a comfortable, quiet, private and closed-door location.	☐ YES	☐ NO
• The Subject was given ample time to read the consent form and opportunity to inquire about details of the research study.	☐ YES	☐ NO
• The Subject was offered the opportunity to take the ICF home and/or to discuss with others.	☐ YES	☐ NO
• The Subject chose to take the ICF home or to discuss with others before making a decision to participate.	☐ YES	☐ NO
• The Subject was encouraged to ask questions regarding the study throughout the Informed Consent Process.	☐ YES	☐ NO
• The randomization method was explained to the subject.	☐ YES	☐ NO
• The subject was asked direct questions regarding their participation, responsibilities during the study and risks. The subject verbalized understanding of all. The subject appears to have a clear understanding of the study procedures and risks.	☐ YES	☐ NO
• All questions were answered / addressed to the subject's satisfaction and understanding.	☐ YES	☐ NO
• Subject voluntarily agrees to participate in the study without coercion or undue influence.	☐ YES	☐ NO
• Version/Date _____/_____ of the IRB approved ICF was signed/personally dated by the Subject and the person conducting the informed consent process today at _____ am / pm, before any study procedures were performed on this date.	☐ YES	☐ NO
• Copy of the signed and dated ICF given to subject.	☐ YES	☐ NO
• Was a witness utilized during the IC process? If yes, explain	☐ YES	☐ NO
• Subject states understanding of research procedures that will be performed at today's visit and all questions have been answered to the subject's satisfaction.	☐ YES	☐ NO
• Subject is able to read and write in the English language.	☐ YES	☐ NO
• The PI _____ is aware of enrollment today.	☐ YES	☐ NO

Return Visit

FLOW CHART

Investigations/Tests and Procedures	SCREENING	RANDOMIZATION	TREATMENT PERIOD[4]												FOLLOW UP PERIOD
Visit Number	1	2	3	4	5	6	7[2]	8	9[2]	10	11[2]	12	13[2]	EOT[3]	FINAL VISIT[3,5]	PHONE CALL[6]
Months since Randomization			3	6	9	12	15	18	21	24	27	30	33			
Time Window (days)[4]	Up to -14 days	0[1]	+/- 14	+/- 14	+/- 14	+/- 14	+/- 14	+/- 14	+/- 14	+/- 14	+/- 14	+/- 14	+/- 14		+/- 14	+/- 14
Informed Consent	X															
Check Eligibility	X	X														
Medical History	X															
Demographics	X															
Confirm Inclusion/Exclusion		X														
Randomization via IRT		X														
Physical Exam	X														X	
Vital Signs (BP, sitting heart rate)[7]	X	X	X	X	X	X		X		X		X		X	X	
ECG[8]	X	(X)		(X)		X		(X)		X		(X)		X	(X)	(X)
Documentation of Cardiac Monitoring[8]	X	(X)	(X)	(X)	(X)	(X)		(X)		(X)		(X)		(X)	(X)	
Pregnancy Test[9] for WOCBP	X		X	X	X	X		X		X		X		X	X	X
Safety Laboratory Tests[10]	X	(X)[10]		X		X		X		X		X		X	X	
Weight	X			X		X		X		X		X		X	X	
Height	X															
PK sample[11]	X	(X)[11]	X			X										
Biomarker (substudy)[12]	X			X												
Plasma sample for assay validation (substudy)[13]	X		X			X										
The Montreal Cognitive Assessment (MoCA)[14]	X														X[15]	

Return Visit (cont'd.)

RETURN VISIT

Visit 4 (6 month)
Subject Initials:_____
Subject Number:_____

NAME OF STUDY
Study: Full Description
PI: John Doe, M.D.
IRB#:

Visit Date: _____

Subject desires to continue participation in study.

INFORMED CONSENT PROCESS (ICP)		
The following person(s)were present for the IC process:		
The study procedure(s) to be performed at today's visit was/were explained by:		
The cognitive ability of the subject was assessed and determined to be capable of making decisions for him/herself	YES	NO
The study procedure(s) to be performed was/were discussed in a comfortable, quiet, private and closed-door location.	YES	NO
The subject was encouraged to ask questions regarding study procedures.	YES	NO
Did the subject request to speak to PI for additional information?	YES	NO
The PI was available to answer questions, if needed.	YES	NO
All questions were answered / addressed to the subject's satisfaction and understanding.	YES	NO
Subject voluntarily agrees to continue participation in the study without coercion or undue influence.	YES	NO

ICF current ☐ Yes ☐ No

If No: Updated Informed Consent Form (version _____) given to subject / LAR. See attached ICP documentation checklist.

Subject desires to continue participation in biomarkers sub-study: ☐ Yes ☐ No ☐ NA

Study procedures completed per protocol:

☐ Pulse: _____ (sitting, palpated w/finger x 60 seconds) □ Regular □ Irregular

Per Subject, have there been any noticeable irregularities in pulse since last visit? □ Yes □No

Blood Pressure assessed per protocol (seated, resting for 5"), machine # _____

R L Arm; _____ / _____ mm/Hg Weight: _____kg lb

☐ Concomitant medications updated (see con med log). Subject reminded not to take any medications listed as "restricted" per protocol. Encouraged to call with questions should new medications or supplements be prescribed.

☐ Subject interviewed / assessed for any adverse events. Subject encouraged to call should any invasive procedures be scheduled or adverse events occur before next visit.

☐ Study medication compliance assessed.

Study Drug or Placebo:_____% ASA or Placebo:_____%

Was compliance for both medications between 80-120%? ☐Yes ☐ No

If no, compliance issues must be addressed and reinforced. Document below.

Has Subject missed any study medications in the last 3 days? ☐Yes ☐ No

If yes, please detail missed study medication:_____

☐ Protocol Safety Laboratory tests drawn per _____, at ____:____ Location_____

Biomarkers drawn: ☐Yes ☐ No ☐ NA

Processed & shipped / stored according to protocol. See specimen logs for details.

☐ Urine pregnancy test completed for women of childbearing potential: Result_____ ☐ NA

Serial #_____ Expiration Date:_____

IVRS contacted to confirm visit, obtain randomization number and kit number for study drug administration during this visit. See attached notification. See stickers below:

[redacted] [redacted] [redacted] Optional [redacted]

IP dispensed per protocol; dose taken at ___:___. Subject given detailed reminders regarding medication, proper storage and dosing schedule. Verbalizes understanding of all instructions. Encouraged to call with questions or concerns. Return appointment made for _____at ___:___. Detailed instructions for return visit given to subject.

_____

_____

_____

Form Completed by:_____Date:_____

Adverse Event Log

Study:									**Subject Initials:**	
PI: John Doe, MD									**Subject ID #:**	
IRB#:										
Event #	**Adverse Event**	**Start Date**	**Stop Date**	**Severity**	**Expected?**	**Related?**	**Intervention**	**Subject withdrawn?**	**Outcome?**	**Investigator Initials & Date**
		:	:							
		:	:							
		:	:							
		:	:							
		:	:							
		:	:							
		:	:							
		Severity:			**Relationship:**	**Intervention:**			**Final Outcome:**	
		1 = Mild			1 = Unrelated	1 = None			1 = Resolved	
		2 = Moderate			2 = Unlikely	2 = Study Treatment dc'd			2 = Resolved w/sequelae	
		3 = Severe			3 = Possible	3 = Drug treatment given			3 = Ongoing	
					4 = Probable	4 = Non-drug treatment given			4 = Lost to follow up	
					5 = Definite				5 = Death	

Concomitant Medication Log

Study: Wonder-Drug
IRB#: 19-12345-FB
PI: John Doe, MD

Subject Initials:_____
Subject ID#:________

Drug Name (Trade name preferred)	Unit Dose	Units	Frequency	Route	Reason for Medication (Indication)	Start Date	Taken Prior to Study?	Ongoing?
						___/___/______	☐ Yes ☐ No	☐ Yes ☐ No End Date: ___/___/______
						___/___/______	☐ Yes ☐ No	☐ Yes ☐ No End Date: ___/___/______
						___/___/______	☐ Yes ☐ No	☐ Yes ☐ No End Date: ___/___/______
						___/___/______	☐ Yes ☐ No	☐ Yes ☐ No End Date: ___/___/______
						___/___/______	☐ Yes ☐ No	☐ Yes ☐ No End Date: ___/___/______
						___/___/______	☐ Yes ☐ No	☐ Yes ☐ No End Date: ___/___/______
						___/___/______	☐ Yes ☐ No	☐ Yes ☐ No End Date: ___/___/______
						___/___/______	☐ Yes ☐ No	☐ Yes ☐ No End Date: ___/___/______
						___/___/______	☐ Yes ☐ No	☐ Yes ☐ No End Date: ___/___/______
						___/___/______	☐ Yes ☐ No	☐ Yes ☐ No End Date: ___/___/______

Comments: ____

Assessment Tool Flowsheet

NIHSS Flowsheet

Subject Number:_____
Subject Initials:_____

Study: Wonder-Drug
PI: John Doe, MD
IRB #: 19-12345-FB

NIH STROKE SCALE ITEM	Screening	2-6 hours	20-36 hours	Unscheduled	5 days or DC	30 days
	Date:	Date:	Date:	Date:	Date:	Date:
	Time:	Time:	Time:	Time:	Time:	Time:
1a. Level of Consciousness (0-3)						
1b. LOC Questions (0-2)						
1c. LOC Commands (0-2)						
2. Best Gaze (0-2)						
3. Visual (0-3)						
4. Facial Palsy (0-3)						
5&6 Motor Arm and Leg:						
5a. Motor Left Arm (0-4 or UN)						
5b. Motor Right Arm (0-4 or UN)						
6a. Motor Left Leg (0-4 or UN)						
6b. Motor Right Leg (0-4 or UN)						
7. Limb Ataxia (0-2 or UN)						
8. Sensory (0-2)						
9. Best Language (0-3)						
10. Dysarthria (0-2 or UN)						
11. Extinction & Inattention (0-2)						
Other neurological findings:	**TOTAL SCORE:**	**TOTAL SCORE:**	**TOTAL SCORE:**	**TOTAL SCORE:**	**TOTAL SCORE:**	**TOTAL SCORE:**
Assessment performed by:						

Your documentation matters!

The research visit note is one piece of the research puzzle.

Your doucmentation is the "glue" that pulls the reserach pieces together!

Common findings related to documentation

- Eligibility criteria could not be confirmed.
- Informed consent process documentation missing or incomplete.
- Discrepancies within records
- Missing information/visits not documented
- AE/SAEs not documented/captured
- ALCOA-C not followed

Benefits of complete documentation

- Documents subject safety and well-being
- Demonstrates understanding of documentation requirments
- Provides confidence in site and study staff by others
- Ensures integrity and credibility of the site/staff/data
- Prepares for favorable monitoring or audit outcomes

Takeaways

- ✓ **"If it wasn't documented, it wasn't done."**
- ✓ **Running, handwritten notes leave room for omissions and human errors.**
- ✓ **The Site Source Doc can serve as a visit checklist.**
- ✓ **Make sure you tell the entire story.**
- ✓ **Your SSD/source should mirror your protocol and CRFs.**