SOP Writing for Clinical Research

Write down what you do, do what is written down!

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My Background

- **Quorum Review IRB**
  - Created sets of SOPs for 4 processes
- **UW Human Subjects Division**
  - Created sets of SOPs for 6 processes
  - Assisted researchers with creating SOPs in response to compliance issues
- **ITHS**
  - Created sets of SOPs for 3 processes
  - Assist researchers with creating SOPs and MOPs
What we will cover

• The differences between SOPs and MOPs
• Importance, Benefits, and Limitations of SOPs
• The 8-Fold SOP Process
  ▫ Process Mapping
  ▫ Authoring
  ▫ Format & Language
  ▫ Editing
  ▫ Authorizing
  ▫ Training
  ▫ Implementing
  ▫ Revising & Archiving
• Caveat: These are the basics!
SOP vs. MOP

Standard Operating Procedures vs. Manual of Procedures
SOP vs. MOP

• Definitions:
  ▫ **Standard Operating Procedures:**
    Detailed, written instructions to achieve uniformity of the performance of a specific function. (ICH GCP 1.55)
  ▫ **Manual of Operations:**
    A handbook of instructions designed to guide the research team to successfully carry out aspects of a research study according to study protocol.
**SOP** vs. **MOP**

- Founded in federal regulations and guidance, Good Clinical Practice guidelines, and institutional policies and guidance
- General processes common to running all studies
- Infrequent changes

- Established in a grant, protocol, and/or IRB application
- Study-specific processes to gather data for one study’s research aims
- Changes throughout the life of the study (updated with each new Modification)
SOPs

Importance
Benefits
Limitations
Importance of SOPs

• Manage compliance obligations
  ▫ Incorporates regulations, GCPs, and institutional requirements

• Create operational efficiency
  ▫ Ensures processes have been examined and optimized

• Training staff
  ▫ Acts as a resource to keep everyone on the same page at all times
Benefits of SOPs

• Creation of:
  ▫ Ensures the team knows their regulatory obligations and how to best meet them using available resources

• Implementation of:
  ▫ Standardizes common processes amongst all studies
  ▫ Provides a level of formal accountability for team members
  ▫ Prevents noncompliance on a systemic level
Benefits of SOPs

- Some thoughts on SOPs in terms of investigations and audits:
  - The process of creating SOPs enhances awareness and working knowledge.
  - Training staff on SOPs ensures everyone is doing things the same way.
  - Should you have an investigation or audit, an SOP-trained staff should have no problems.
  - Should you have an investigation and no SOPs, you could be vulnerable to findings.
- Results of most audits usually include recommendations or requirements to create SOPs.
Limitations of SOPs

They can’t help you if you don’t use them.
How many SOPs are we talking?

- Research teams should have SOPs to cover the following topics, at minimum:
  1. Recruitment and Retention of Participants
  2. Informed Consent Process
  3. Filing and Recordkeeping
  4. IRB Review: Initial, Modification, and Continuing Review
  5. Documenting, Resolving, and Reporting Protocol Deviations and Violations, Adverse Events, and Unanticipated Problems
  6. Study Closure
  7. SOP for SOPs (aka, the 8-Fold SOP Process)
The 8-Fold SOP Process

1. Process Mapping
2. Authoring
3. Format & Language
4. Editing
5. Authorizing
6. Training
7. Implementing
8. Revising & Archiving
Step 1: Process Mapping

- Start with the **regulations, guidance, and institutional policy:**
  - **Regulations**
    - OHRP: 45 CFR 46, and FDA: 21 CFR 50, 56, and 312
  - **Guidance**
    - ICH GCPs
    - OHRP and FDA Guidance
  - **Institutional Policy**
    - UW: Faculty Handbook and Human Subjects Division
    - Childrens: Office of Research Compliance and IRB
    - FHCRC: Institutional Review Office
Process Mapping Example

- Documenting, Resolving, and Reporting Protocol Deviations and Violations at UW
  - OHRP & FDA:
    - 45 CFR 46.103(b)(4)(iii) and 21 CFR 56.108(a)(4)
  - ICH GCPs:
    - ICH GCP 4.5.2-4.5.4
  - UW Faculty Handbook:
    - UW Faculty Handbook, Volume 4, Part 2, Chapter 2, Section 5.E.
  - UW Human Subjects Division
    - Form “Report of Other Problems,” document K-324
Step 1: Process Mapping

- Next, set up a **meeting** with everyone involved in the process
- Think about **your experience** with the process
- Present **regulatory background** and your experience at the meeting.
  - Talk with the group about their **experiences** with the process.
  - Choose the best **author** for the process.
  - Set up a future meeting to finalize the SOP, with a **draft SOP** to be circulated in advance by the author.
Step 2: Authoring

- Who’s the best person to write what you do?
  - The person who does it.
Step 3: Format & Language

- Design a template format that includes at least the following elements:
  - SOP title
  - Purpose statement
  - Policy statements, definitions, etc.
  - Steps to complete process
  - Version # and effective date
  - Author signature and date
  - Authorizer signature and date
  - References
Step 3: Format & Language

- When writing SOPs, make sure the language is **clear** and **concise**:
  - Use short, active sentences
  - Simple words
  - Instructional tone
Step 3: Format & Language

- When writing, be sure to:
  - Put tasks in correct **order**
  - Use **titles**, not names
  - **Limit** number of steps per page
  - Include **timelines** for completion of tasks
  - Reference associated **forms** and **templates**
Step 3: Format & Language

Documenting, Resolving, and Reporting Protocol Deviations and Violations Procedure

PURPOSE
To describe the process of recording, resolving, and reporting protocol deviations and violations.

POLICY
According to federal regulations and the Collaborative IRB Policy, each site is responsible for ensuring that any deviations from the approved research data quality plan is identified, documented, and reported within 14 days of the deviation.

DEFINITIONS
The following are defined for the purposes of this policy:

1. A protocol deviation is any condition that occurs during the conduct of the study, which has a potential to impact the accuracy of the data.

Example: A deviation occurs when a subject is enrolled in the study but the inclusion criteria are not met, or data is collected incorrectly.

2. A protocol violation is any action that violates the approved protocol.

Example: Failure to obtain informed consent or failure to follow the study protocol.

PROCEDURE
1. Identification: Each occurrence of any deviation or violation is identified and documented.

Example: Documenting the deviation in the Protocol Deviation Log.

2. Resolution: Resolve the deviation or violation as outlined in the approved protocol.

Example: Revising the protocol to address the deviation.

3. Reporting: Report the deviation or violation to the IRB and appropriate regulatory authorities.

Example: Submitting the protocol deviation report to the IRB.

REFERENCES
- 45 CFR 46.115
- 21 CFR 50.2
- 21 CFR 50.6
- University of Health Sciences, Research Committee
- The National Institutes of Health
- The Research Protocol Violation Log

Annexure:

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Records a protocol deviation or violation.
Step 3: Format & Language

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<th>Date(s) of Deviation</th>
<th>Deviation Description (including involved subject(s) study ID)</th>
<th>Deviation Resolution Description (including date of resolution)</th>
<th>Date Reported to Sponsor (if funded)</th>
<th>Date Reported to IRB</th>
<th>Action Required by Sponsor and/or IRB (state &quot;none&quot; if no action required)</th>
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Step 4: Editing

- Who should edit the draft SOP?
  - The **group** who originally met.

- Process:
  - Circulate the **draft** pre-meeting.
  - Reach group **consensus** about the draft changes.
  - Take good **notes** about agreed upon changes.
  - Revise the draft.
  - Recirculate to the group and ask for feedback by a **firm date**.
Step 4: Editing

• Process (con’t):
  □ After recirculating, incorporate feedback to finalize SOP.
  • If necessary, reconvene for another meeting.
  □ Have another team member edit the SOP using a Quality Assurance Checklist.

SOP Quality Assurance Checklist

Check each box to confirm the following statements:

- The title is accurate and descriptive of the SOP.
- The purpose of the SOP is accurate.
- The version and date are accurate.
- If a revision, these have been updated.
- SOP is in active voice (not passive voice).
- Language is simple.
- Ordering of tasks make sense and includes all necessary steps to complete process.
- If appropriate, alternative formats (flow charts, diagrams, narratives, tables, bullet lists, footnotes) are utilized effectively.
- Sources and references provided are accurate.
- Spell check is complete.
- The author signed the SOP.
- The person authorizing the SOP signed the SOP.

Name of person completing checklist: __________________________ Date: ____________
Step 5: Authorizing

- Since the **Principal Investigator** is ultimately responsible for the conduct of the study, he/she should be the one who **authorizes all SOPs**.
  - The author should **sign and date** the original SOP, and so should the PI.
Step 6: Distributing

- **PDF** the signed original.
- Place the **hard-copy signed original** in an SOP binder.
- Keep the **electronic original** in a secure location.
- Choose a place to **post PDF SOP** for reference:
  - Internet / Intranet
  - Server
  - Email
  - Paper
Step 6: Distributing

- **Identify** team members who are part of the process
- **Notify** them that there is a new SOP
Step 7: Training

• The most important step!
  ▫ If training doesn’t happen effectively, the SOPs are useless.

• Choose the best training approach for the SOP:
  ▫ One-on-one
  ▫ Group
Step 7: Training

• Have the **author** train other team members on the SOP.

• **Document** team members’ training completion
  - ITHS Study Team Training Log
    - [www.iths.org/forms](http://www.iths.org/forms)
Step 8: Revising & Archiving

• What happens if a mistake is found, or if the regulations or policies change?
  ▫ You must have a **formal revision process** that includes:
    • A **designated** member of the study team to manage this process
    • A secured **document management system** (create audit trails, use track changes)
    • A policy on whether revisions are done on a **rolling basis** or at **established time points**, or both
Step 8: Revising & Archiving

- When SOPs are updated, the old versions need to be archived for historical reference.
  - Keep all hard-copy signed originals in the SOP binder
  - Label superseded versions as “Archived” (stamp or handwritten)
  - Remove superseded PDF versions from circulation
Resources

- ITHS Research Coordinator Core
  - [http://www.iths.org/node/450](http://www.iths.org/node/450)
- OHRP
  - [http://www.hhs.gov/ohrp/](http://www.hhs.gov/ohrp/)
- FDA
  - [http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm155713.htm](http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm155713.htm)
- ICH GCP
  - [www.ich.org/LOB/media/MEDIA482.pdf](http://www.ich.org/LOB/media/MEDIA482.pdf)
- ITHS forms
  - [http://www.iths.org/forms](http://www.iths.org/forms)
Summary

I hope you will walk away with an appreciation of the following:

- SOPs are general processes that apply to all studies.
- They are tools for efficiency and compliance.
- Regular use and revision of SOPs is paramount.
- The 8-Fold SOP Process to develop SOPs.
Questions?