SOP Writing for Clinical Research

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

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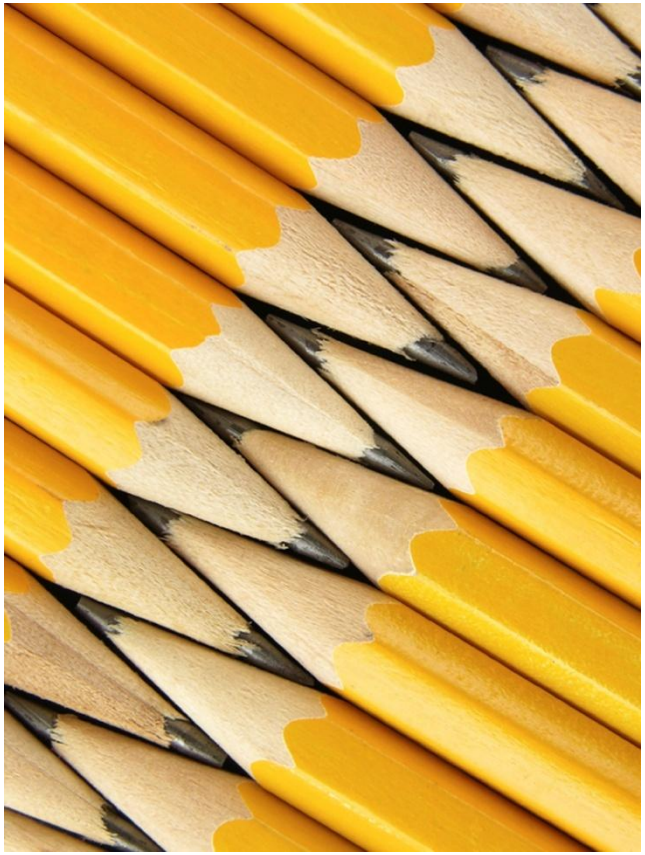
My Background

- 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 **O**perating **P**rocedures

vs.

Manual **o**f **P**rocedures

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

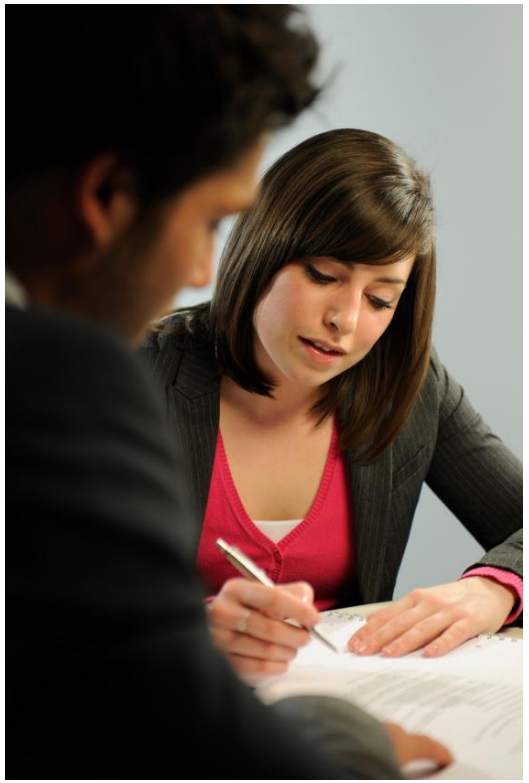
- Documenting, Resolving, and Reporting Protocol Deviations and Violations at UW
  - OHRP & FDA:
    - 45 CFR 46.103(b)(4)(iii) and 21 CFR 56.108(a)(4)
  - ICH GCPs:
    - ICH GCP 4.5.2-4.5.4
  - UW Faculty Handbook:
    - UW Faculty Handbook, Volume 4, Part 2, Chapter 2, Section 5.E.
  - UW Human Subjects 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.

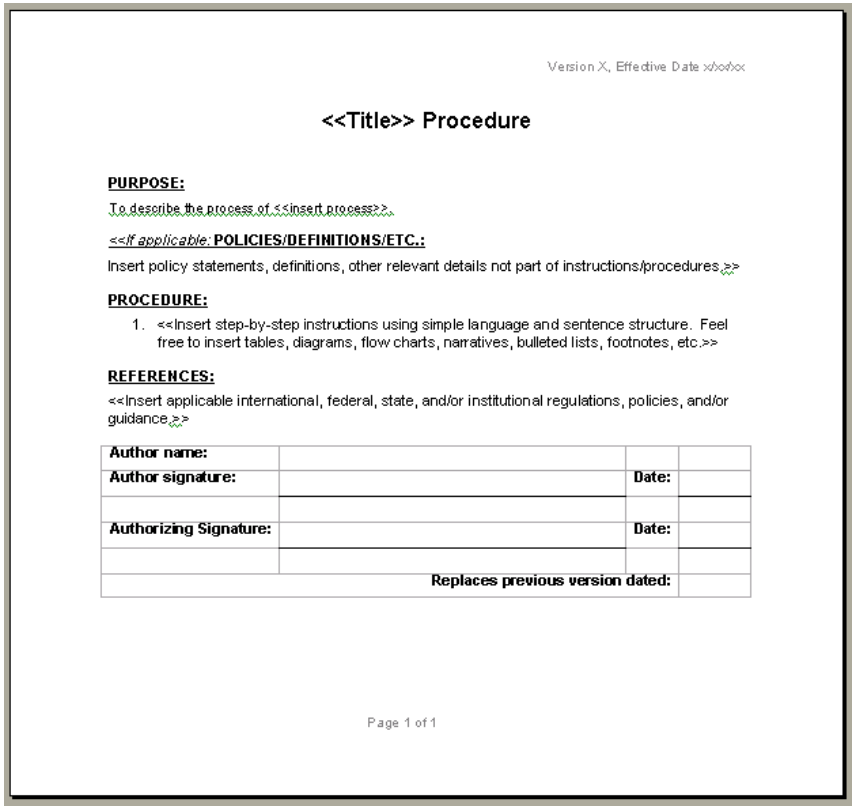
Step 2: Authoring

- 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



Version X, Effective Date xx/xx/xx

<<Title>> Procedure

PURPOSE:

To describe the process of <<insert process>>.

<<If applicable: **POLICIES/DEFINITIONS/ETC.:**

Insert policy statements, definitions, other relevant details not part of instructions/procedures.>>

PROCEDURE:

1. <<Insert step-by-step instructions using simple language and sentence structure. Feel free to insert tables, diagrams, flow charts, narratives, bulleted lists, footnotes, etc.>>

REFERENCES:

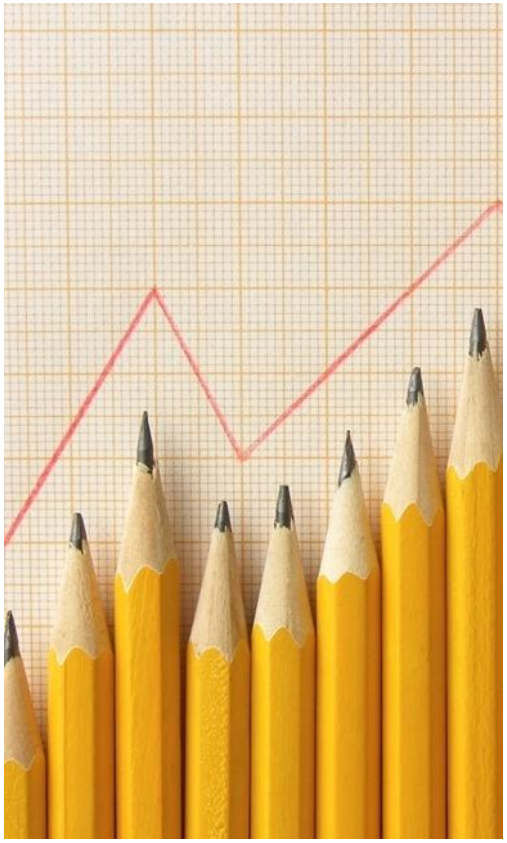
<<Insert applicable international, federal, state, and/or institutional regulations, policies, and/or guidance.>>

Author name:			
Author signature:		**Date:**	
Authorizing Signature:		**Date:**	
		Replaces previous version dated:	

Page 1 of 1

Step 3:
Format & Language

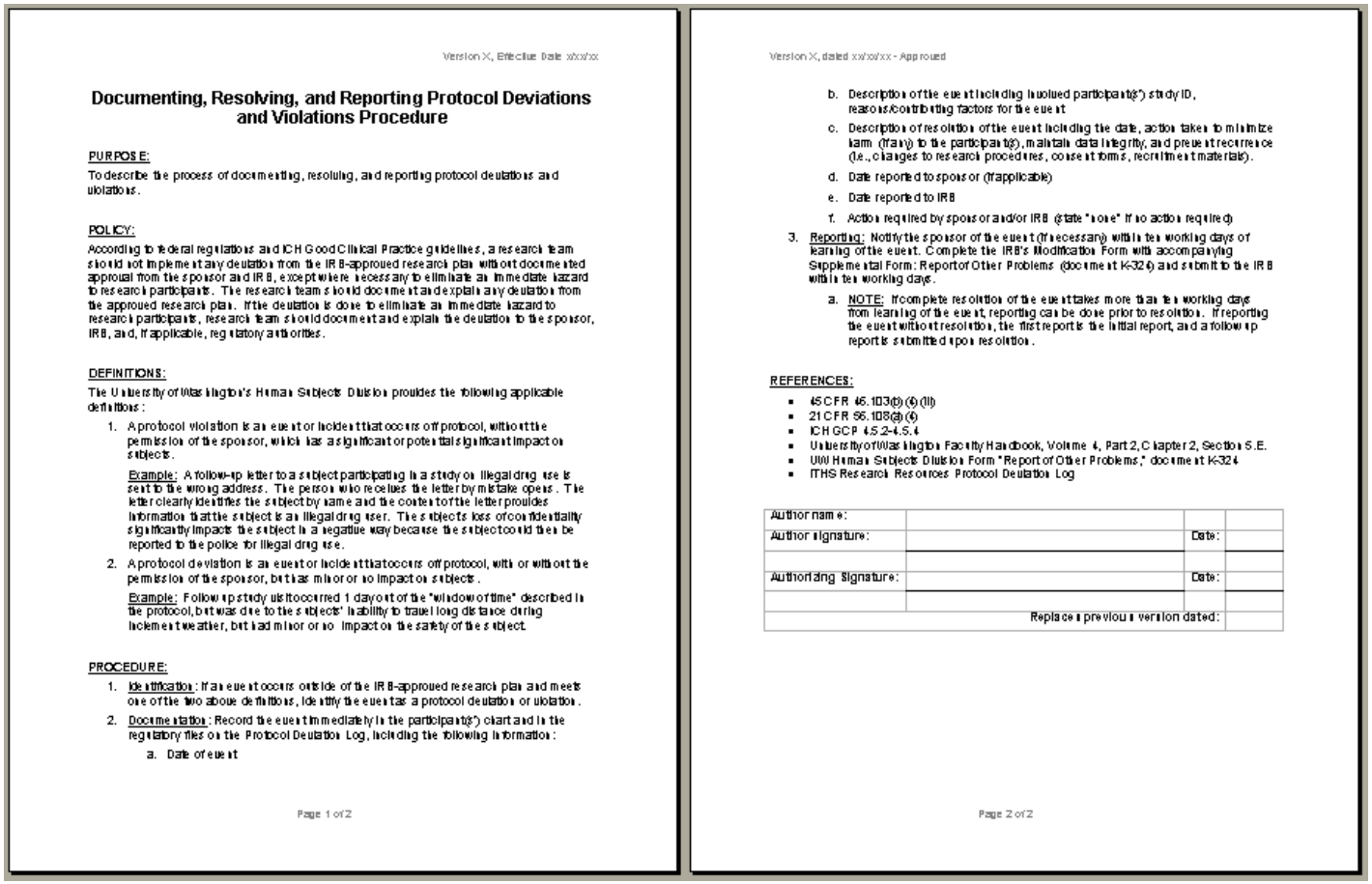
- When writing SOPs, make sure the language is **clear** and **concise**:
  - Use short, active sentences
  - Simple words
  - Instructional tone



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



Version X, Effective Date xx/xx/xx

Documenting, Resolving, and Reporting Protocol Deviations and Violations Procedure

PURPOSE:

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

POLICY:

According to federal regulations and ICH Good Clinical Practice guidelines, a research team should not implement any deviation from the IRB-approved research plan without documented approval from the sponsor and IRB, except where necessary to eliminate an immediate hazard to research participants. The research team should document and explain any deviation from the approved research plan. If the deviation is done to eliminate an immediate hazard to research participants, research team should document and explain the deviation to the sponsor, IRB, and, if applicable, regulatory authorities.

DEFINITIONS:

The University of Washington's Human Subjects Division provides the following applicable definitions:

1. A protocol violation is an event or incident that occurs off protocol, without the permission of the sponsor, which has a significant or potential significant impact on subjects.

   Example: A follow-up letter to a subject participating in a study on illegal drug use is sent to the wrong address. The person who receives the letter by mistake opens. The letter clearly identifies the subject by name and the content of the letter provides information that the subject is an illegal drug user. The subjects loss of confidentiality significantly impacts the subject in a negative way because the subject could then be reported to the police for illegal drug use.

2. A protocol deviation is an event or incident that occurs off protocol, with or without the permission of the sponsor, but has minor or no impact on subjects.

   Example: Follow up study visit occurred 1 day out of the "window of time" described in the protocol, but was due to the subjects' inability to travel long distance during inclement weather, but had minor or no impact on the safety of the subject.

PROCEDURE:

1. Identification: If an event occurs outside of the IRB-approved research plan and meets one of the two above definitions, identify the event as a protocol deviation or violation.
2. Documentation: Record the event immediately in the participant(s') chart and in the regulatory files on the Protocol Deviation Log, including the following information:
   a. Date of event

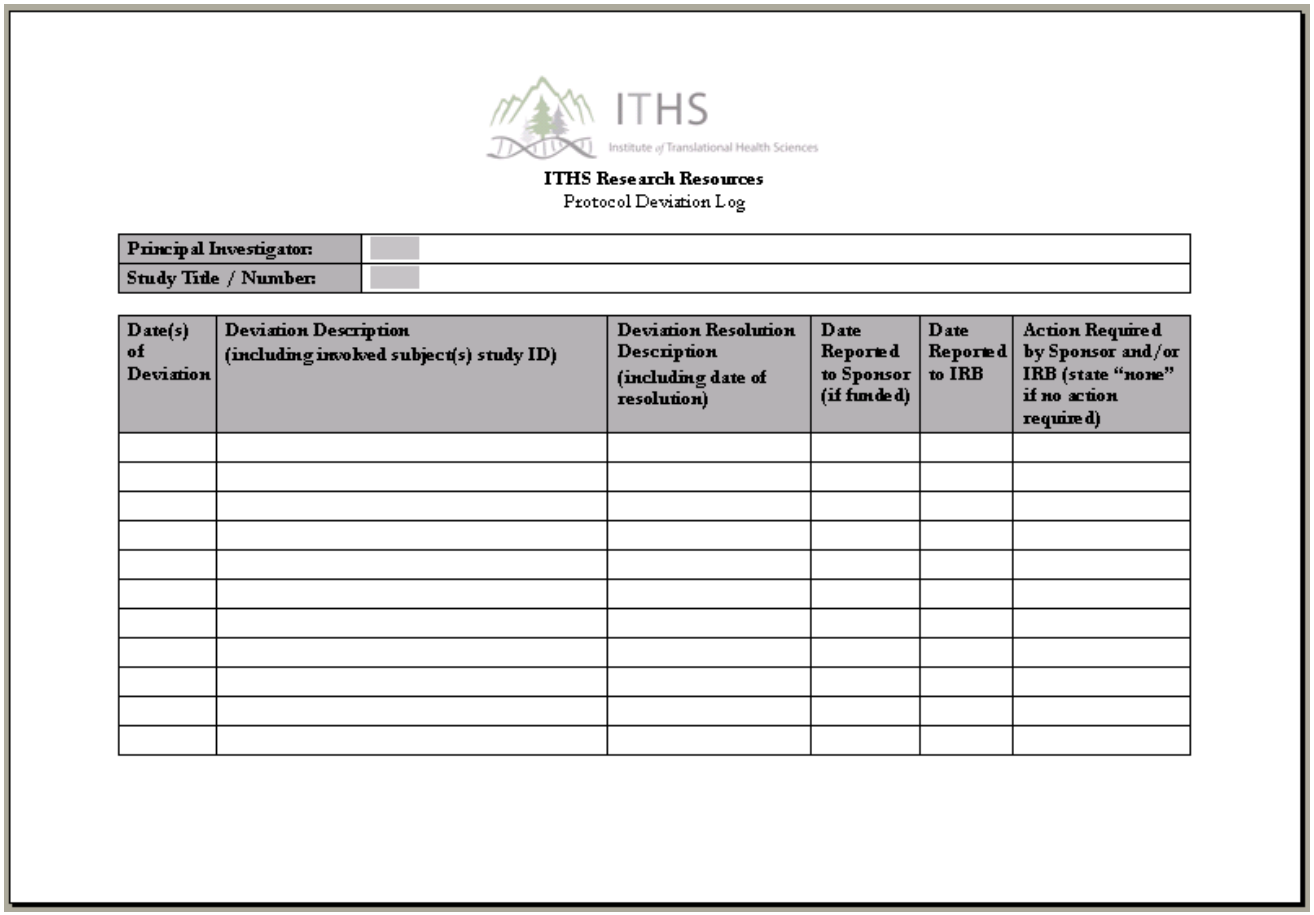
   b. Description of the event including involved participant(s') study ID, reasons/contributing factors for the event
   c. Description of resolution of the event including the date, action taken to minimize harm (if any) to the participant(s), maintain data integrity, and prevent recurrence (i.e., changes to research procedures, consent forms, recruitment materials).
   d. Date reported to sponsor (if applicable)
   e. Date reported to IRB
   f. Action required by sponsor and/or IRB (state "none" if no action required)
3. Reporting: Notify the sponsor of the event (if necessary) within ten working days of learning of the event. Complete the IRB's Modification Form with accompanying Supplemental Form: Report of Other Problems (document K-324) and submit to the IRB within ten working days.
   a. NOTE: If complete resolution of the event takes more than ten working days from learning of the event, reporting can be done prior to resolution. If reporting the event without resolution, the first report is the initial report, and a follow up report is submitted upon resolution.

REFERENCES:

- 45 CFR 46.103(b)(4)(iii)
- 21 CFR 56.108(a)(4)
- ICH GCP 4.5.2-4.5.4
- University of Washington Faculty Handbook, Volume 4, Part 2, Chapter 2, Section 5.E.
- UW Human Subjects Division Form "Report of Other Problems," document K-324
- ITHS Research Resources Protocol Deviation Log

Author name:			
Author signature:		Date:	
Author/irding Signature:		Date:	
		Replaces previous version dated:	

Step 3: Format & Language



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ITHS Research Resources
Protocol Deviation Log

Principal Investigator:	
Study Title / Number:	

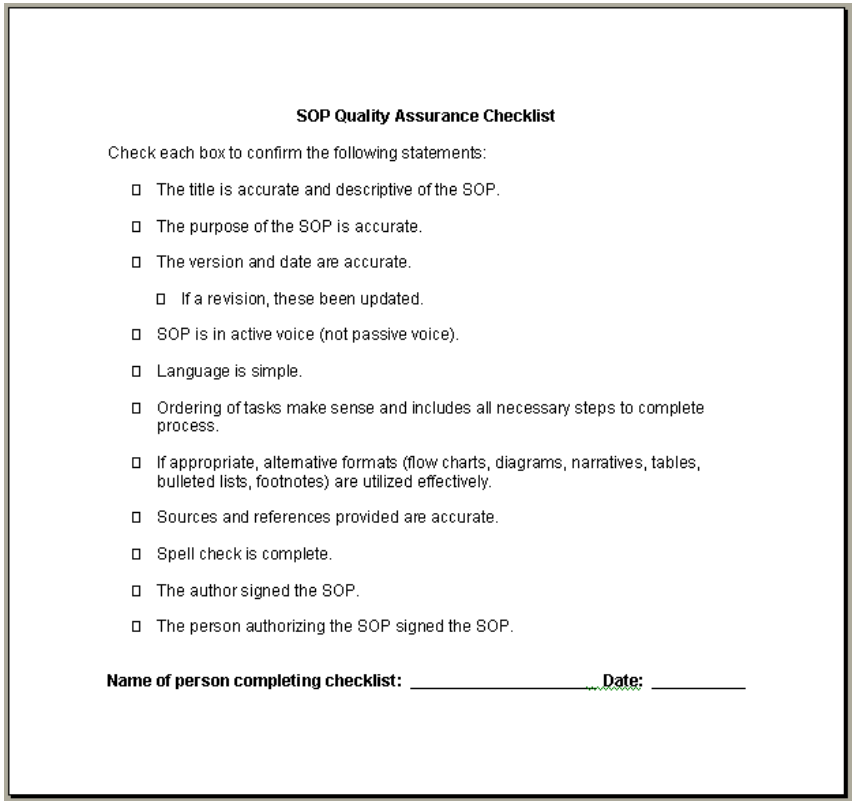
Date(s) of Deviation	Deviation Description (including involved subject(s) study ID)	Deviation Resolution Description (including date of resolution)	Date Reported to Sponsor (if funded)	Date Reported to IRB	Action Required by Sponsor and/or IRB (state "none" if no action required)

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 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, bulleted 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.

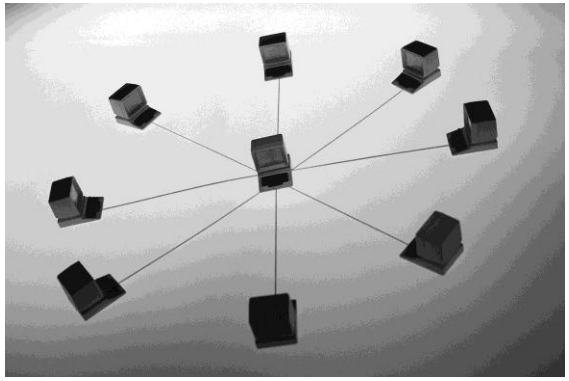
Name of person completing checklist: _____ **Date:** _____

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

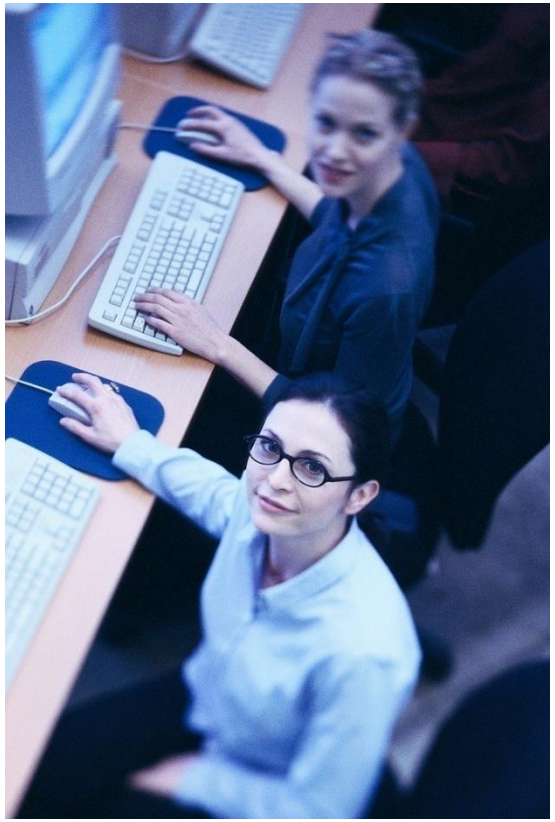


Step 6: Distributing

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

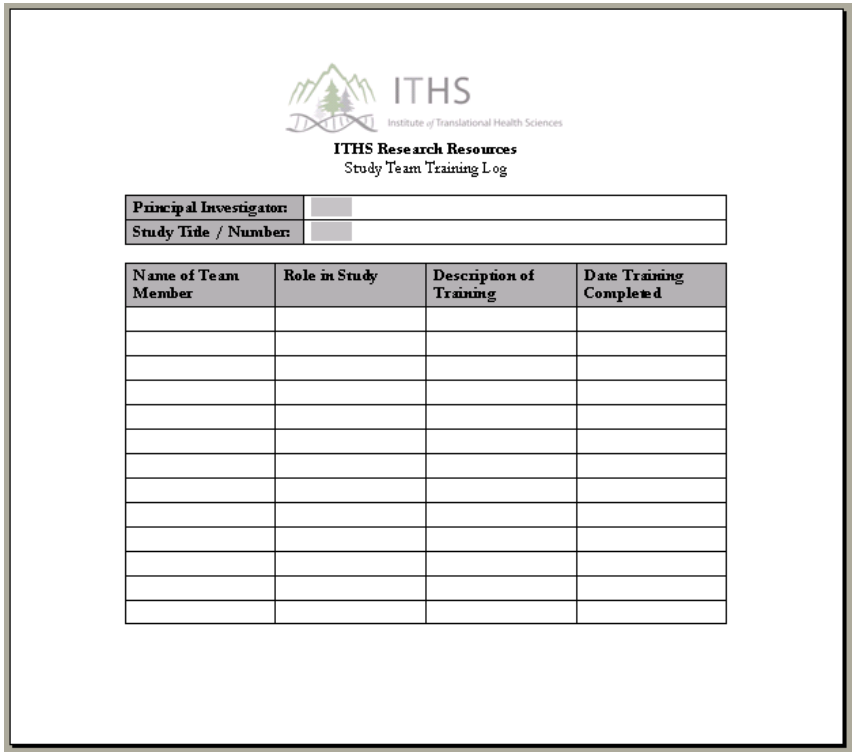
Step 7: Training

- **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



ITHS
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ITHS Research Resources
Study Team Training Log

Principal Investigator:	
Study Title / Number:	

Name of Team Member	Role in Study	Description of Training	Date Training Completed

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
- OHRP
  - http://www.hhs.gov/ohrp/
- FDA
  - http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm155713.htm
- ICH GCP
  - www.ich.org/LOB/media/MEDIA482.pdf
- ITHS 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?