INTRODUCTION

Clinical research, an essential link between basic science and medical therapy, continues to evolve as regulations are revised and new technology is applied. Once the province of the academic medical center, pursued as an adjunct to academic and professional responsibilities such as teaching or basic research, the conduct of clinical research has become both a profession and a business. As clinical research continues to expand into a global enterprise, strict international requirements for standardization, consistency and compliance have become critical.

As clinical trials have become more complex and regulations have become more stringent, programs are faced with the challenge of meeting rigorous standards in a world of diminishing resources. In such an environment, a solid understanding of Good Clinical Practices (GCPs) and their applications is essential. *Standard Operating Procedures for the Conduct of Clinical Research* has been developed and revised to help clinical research sites meet this challenge.

This template builds on the original version, published in 1998 and revised in 2008 and 2014. This updated edition continues to address the application of new technology and guidance documents that have changed or been issued within the last four years.

The 2018 edition includes SOP amendments and updates with reference to and application of the following updates and additions:

- 21 CFR 812.100—General responsibilities of investigators
- Protocol Waivers: Update to investigator requested change or deviation from the protocol or investigational plan
- Payment and Reimbursement to Research Subjects—Information Sheet, January 25, 2018
- Guidance for IRBs, Clinical Investigators, and Sponsors—Considerations When Transferring Clinical Investigation Oversight to Another IRB, May 2014
- Guidance for IRBs, Clinical Investigators and Sponsors, July 2014
- Factors to Consider When Making Benefit-Risk Determinations for Medical Device Investigational Device Exemptions—Guidance for Investigational Device Exemption Sponsors, Sponsor-Investigators and Food and Drug Administration Staff, January 2017
- FDA Decisions for Investigational Device Exemption Clinical Investigations—Guidance for Sponsors, Clinical Investigators, Institutional Review Boards and Food and Drug Administration Staff, August 2014
- Use of Electronic Informed Consent Questions and Answers—Guidance for Institutional Review Boards, Investigators and Sponsors, December 2016
- Guidance for Industry—Use of Electronic Records and Electronic Signatures in Clinical Investigations, July 2018
- Information Sheet Guidance for Institutional Review Boards, Clinical Investigators and Sponsors Clinical Investigator Administrative Actions – Disqualification, March 2014

- Guidance for Industry Circumstances that Constitute Delaying, Denying, Limiting or Refusing a Drug Inspection, October 2014
- Gifts to FDA: Evaluation and Acceptance: Guidance for the Public and FDA Staff, December 2016
- E6(R2): Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice
- PHS: 42 CFR Part 50 Subpart F (Grants): Promoting Objectivity in Research
- Requirement for institutions receiving PHS funding to implement a written policy on financial conflicts of interest and make such policy available via a publicly accessible website.

This edition includes an SOP on the application of root cause analysis and corrective and preventive actions (CAPA) as applicable to issues identified through internal quality assurance, monitoring or audit findings from Sponsor, CRO or regulatory audits and an SOP on the maintenance of electronic medical records (EMRs) and applications to clinical research. In addition, the study feasibility section was enhanced, and SOP training and revision requirements and processes for conducting studies managed through risk-based monitoring were added. The templates were designed to ensure consistency in format and content within a series, which included:

- Policies and Standard Operating Procedures for the Institutional Review Board,
- Standard Operating Procedures for Good Clinical Practice by Sponsors of Clinical Trials,
- Standard Operating Procedures for Privacy Rule Compliance at the Investigative Site.

Institutions can integrate uniform SOPs into the three most important realms for the conduct of clinical research: the Sponsor, the Investigator and the IRB.

Using Standard Operating Procedures for the Conduct of Clinical Research

This template is divided into six general areas that serve as the framework for SOPs.

1. **General Administration SOPs** include procedures essential to conduct a business and that have a broad application to site administration. These SOPs address topics such as delegation of responsibility, document development, personnel issues, contracts, training and communications.
2. **Regulatory Affairs SOPs** include the procedures to ensure that investigative sites operate in a manner consistent with regulatory mandates. In the United States, clinical research usually is overseen by the FDA, OHRP and/or the funding agency. The procedures, generally, focus on ensuring that required applications and reports, along with supporting material and documentation, are submitted as required.
3. **Project Management SOPs** ensure that each clinical trial is well managed. This section addresses the activities unique to the conduct of clinical research that must occur before the study starts, while it is active and after it ends. Therefore, it includes budget development, meeting preparation, source documentation, application of EMRs, protocol compliance and development of corrective and preventative action plans.
4. **Subject Management SOPs** include the range of activities that involve or are related to research subjects. The SOPs focus on two areas: processes that involve interactions with subjects that generate data and those that are meant to protect the welfare of subjects. Activities such as recruitment, the process of informed consent and privacy practices are included.
5. **Data Management SOPs** focus on the routine handling of data captured during the conduct of a clinical study. Considerations for data management in a risk-based monitoring and electronic data environment are included.

6. **Quality Assurance SOPs** address the conduct of internal and third-party audits. Also included are SOPs and detailed checklists to prepare for and manage FDA inspections.

An extensive library of narrative guidelines, checklists, logs and other forms to ensure complete and documented compliance is included. Except for forms required by the FDA, the attachments, like the SOPs, may be used as-is, modified or replaced with preferred forms.

Each SOP is organized into seven sections that move from a general policy statement to the specifics of performing tasks that implement the policy. These seven sections are:

1. Policy—the overall principal that the procedures implement
2. Scope—the extent of the activities addressed by the SOP
3. Responsibility—the titles of the individuals who ensure that the procedures are carried out as required
4. Applicable Regulations and Guidelines—cites the regulations and guidance that dictate the requirement for the policy
5. Associated Attachments—lists the forms, templates and checklists that manage and document the integration of specific procedures into day-to-day activities
6. Process Overview—summarizes the activities addressed in detail in the procedure section
7. Specific Procedures—details the steps to implement the policy.

Editing the Template
This SOP template has been written to be edited and customized for each research site's own use.

1. Getting started - A good way to get started is to search for and replace the following designations:

   <<Site>> and replace with the name of your company or institution.

   <<Designee>> and replace with the title(s) of the individual(s) responsible for the particular activity. Please note, SOPs are meant to be generic and not specific to individuals, so titles for the responsible job function should be used. Do not use individuals' names.

   You will be required to indicate the responsible party for each activity, or group of activities, listed in Section 7 of each SOP, "Specific Procedures." The term << Designee>> appears at the first activity only, but pertains to each activity.

   In general, the symbols << >> enclose words or phrases that should be replaced.

2. The Table of Contents includes page numbers, but the numbers may change when the template is customized. For the same reason, manual page breaks have been used sparingly in the electronic file. Therefore, the pagination in the printed copy may not always match the pagination in the electronic file.

IMPORTANT NOTE FOR SOP IMPLEMENTATION: ONCE SOPS ARE IMPLEMENTED AT YOUR SITE, IT IS IMPORTANT THAT THEY ARE FOLLOWED AS THEY HAVE BEEN WRITTEN AND ANY VARIATION IN ACTIVITIES IS ADDRESSED IN WRITING AS A DEVIATION FROM INTERNAL PROCEDURE REQUIREMENTS WITH A REASON FOR THE DEVIATION AND A CORRECTIVE AND PREVENTIVE ACTION INDICATED TO ENSURE FUTURE ADHERENCE TO WRITTEN OPERATING PROCEDURES. YOUR COMPANY OR INSTITUTION SHOULD REVIEW SOPS AND DEVIATIONS FROM THOSE SOPS ON A REGULAR BASIS. IF DEVIATIONS OCCUR FOLLOWING IMPLEMENTATION OF A CORRECTIVE AND PREVENTIVE ACTION, THEN THE DEVIATION MAY WARRANT REVIEW OF THE CURRENT SOP AND APPLICABLE GUIDANCE/REGULATIONS, AMENDMENT OF THE SOP AND EDUCATION OF ALL APPLICABLE RESOURCES.

About the Author

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Since 1992, Anthony Robinson has worked within clinical operations, regulatory, product strategy and business development at various companies, including Covance, Shire and Barclay Consulting. He has led clinical trial and portfolio programs, submitted multiple pharmaceutical regulatory applications across various therapeutic areas, managed various collaborative service and site providers, executed market/business analyses and worked with teams to establish and optimize industry and regulatory compliant operating processes. www.barclay.consulting.com